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Synthesis of Substituted Thiophene-1,1-Dioxides and their Ring-Opening Reactions with ω-Unsaturated Secondary Amines; a Synthetic Route to Azatrienes.

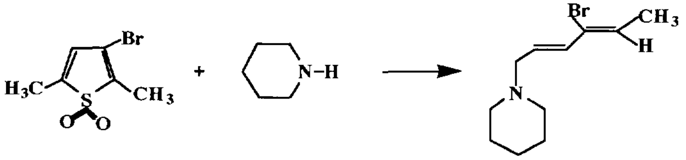
Anders Tsirk, Salo Gronowitz* and Anna-Britta Hörnfeldt

Organic Chemistry 1, Chemical Center, University of Lund, Box 124, S-221 00 Lund, Sweden

Abstract: The scope and limitations of the ring-opening of thiophene dioxides upon reaction with cyclic secondary amines, leading to dialkylaminomethyl substituted halobutadienes has been further studied. Using ω-unsaturated acyclic secondary amines trienes could be prepared by this methodology.

It has previously been found that the reaction of 2,5-dialkyl-3-halothiophene-1,1-dioxides with cyclic secondary amines like piperidine, pyrrolidine or morpholine in toluene at 100 °C stereosectively leads to only one of the four possible dialkylaminomethyl substituted halobutadienes.[1] We were interested in further developing this synthetically useful reaction having other substituents than bromine or chlorine in the 3-position. It was found that 2,5-dimethyl-3-trimethylsilylthiophene-1,1-dioxide also underwent ring-opening upon reaction with piperidine yielding 3-trimethylsilyl-6-piperidino-(2*Z*,4*E*)-2,4-hexadiene.[2] Also some other silyl-substituted derivatives as 2-methyl-5-dimethylbutylsilylthiophene-1,1-dioxide underwent this type of reaction.[2] However, plans to carry out the same reaction with 2,5-dimethyl-3-stannylthiophene-1,1-dioxide could not be realized, as attempts to oxidize 2,5-dimethyl-3-stannylthiophene to the 1,1-dioxide only led to destannylation.[2]

Scheme 1

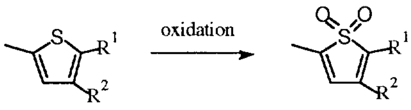


Results and Discussion

In the present paper, some attempts to widen the scope of the amine-induced ring-opening of thiophen-1,1-dioxides by using non-cyclic unsaturated amines, as well as other substituents on the thiophene ring have been made. We also investigated some alternative methods for the oxidation of thiophenes using 2,5-dimethyl-3-bromothiophene (**1**) as a model substance. The results are summarized below:

1. **1**:SeO_2:H_2O_2 (molar ratio 1:3:6) in methanol, 0-25 °C, 40 h, yield 24 %.[3]
2. **1**:Me_3NO:OsO_4 (molar ratio 1:3:0.05) in THF/*t*-BuOH, 25 °C, 24 h, yield < 3 % (GLC).[4]
3. **1**:Ethyl cyanoformate:H_2O_2 (molar ratio1:2.4:3) in acetonitrile, 25 °C, 40 h, yield 24 % (GLC).[5]

Scheme 2



1-8 **9-16**

It is evident that none of these methods is as good as the standard procedure in which *meta*-chloroperbenzoic acid is used as oxidizing agent[6] and which gives 3-bromo-2,5-dimethylthiophene-1,1-dioxide (**9**) in 59 % yield. The dioxides of 2,5-dimethyl-3-trimethylsilylthiophene (**2**), 2-methyl-5-(*t*-butyldimethylsilyl)-thiophene (**4**) 3-bromo-5-methyl-2-trimetylsilylthiophene(**5**) and 3-bromo-2-isopropyl-5-methylthiophene could also be synthesized according to this procedure. In this way 2,5-dimethyl-3-trimethylsilylthiophene-1,1-dioxide (**10**),[2] 2-methyl-5-(t-butyldimethylsilyl)thiophene-1,1-dioxide (**12**),[2] 3-bromo-5-methyl-2-trimethylsilylthiophene-1,1-dioxide (**13**) and 3-bromo-2-isopropyl-5-methylthiophene-1,1-dioxide (**14**)[7] were obtained in 79 %, 74 %, 74 % and 3 9 % yield respectively (Table I).

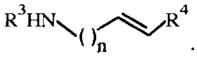
Table 1. Isolated yield (%) of some oxidized thiophene derivatives (**1-8**) in dichloromethane.

Thiophene	Thiophene-1,1-dioxide	Oxidant	R^1	R^2	Isolated yield (%)
1	**9**	*m*-CPBA	Me	Br	59
2	**10**	-"-	Me	$SiMe_3$	79
3	**11**	-"-	Me	H	39
4	**12**	-"-	Si-t-$BuMe_2$	H	74
5	**13**	-"-	$SiMe_3$	Br	74
6	**14**	-"-	i-Pr	Br	39
7	**15**	DMD	Me	$SnMe_3$	65
8	**16**	-"-	Me	$OSi(i\text{-}Pr)_3$	25

However, these acidic reaction conditions were not suitable for the oxidation of 2,5-dimethyl-3-trimethylstannylthiophene (**7**) or of 2,5-dimethyl-3-trimethylsilyloxy thiophene (**8**). Instead, a method using a dilute solution of dimethyldioxirane in acetone was found to be the one of choice, the dioxirane was synthesized from potassium peroxymonosulfate (oxone) and acetone and distilled from the reaction mixture, when a slight *vacuum* was applied to the reaction vessel.[8] Thus 2,5-dimethyl-3-trimethylstannylthiophene-1,1-dioxide (**15**) was synthesized in 65 % yield and 2,5-dimethyl-3-triisopropylsiloxythiophene-1,1-dioxide (**16**) in 25 %.

Compound **8** was prepared by silylation of 2,5-dimethyl-3-hydroxythiophene[9] according to a method described by Corey *et al.*[10] The other necessary thiophenes were prepared by literature procedures and in the following way. Halogen-metal exchange between 2,3-dibromo-5-methylthiophene and butyllithium followed by reaction with trimethylsilyl chloride gave 3-bromo-5-methyl-2-trimethylsilythiophene (**5**) in 64 % yield, adding acetone gave 3-bromo-2-isopropenyl-5-methylthiophene, which was hydrogenated over Wilkinson's catalyst to give 3-bromo-2-isopropyl- 5-methylthiophene (**6**) in 71 % yield.[9]

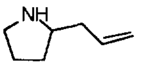
The unsaturated amines were obtained as follows: *N*-allylmethylamine (**17**) was commercially available from Fluka. *N*-(3-butenyl)-methylamine (**18**) was synthesized according to Courtois *et al.* [11] *via*

Table 2. Overall yields (%) for some unsaturated amines, .

Amine	n	R^3	R^4	Yield (%)	Reference for procedure
17	1	Me	H	commercial	
18	2	Me	H	32	11
19	3	Me	H	22	12
20	1	Bz	H	56	12
21	2	Me	COOEt	0.8	13
22	1	Bz	COOEt	18	13

an allylzinc bromide alkylation of *N*-chloromethyl-*N*-methylformamide and subsequent hydrolysis of the so produced *N*-(3-butenyl)-*N*-methylformamide by a 10 % aqueous potassium hydroxide solution, *N*-(4-pentenyl)-methylamine (**19**) was obtained by way of *N*-alkylating the trifluoroacetamide anion with 1-bromo-4-pentene in a refluxing tetrahydrofuran-potassium hydride solution,[12] followed by hydrolysis as described above. The same method was used to synthesize *N*-allylbenzylamine (**20**). Momose *et al.* provided the route for synthesizing the more complex amines ethyl-1-amino-*N*-methyl-2-pentenoate (**21**) and ethyl-1-amino-*N*-benzyl-2-butenoate (**22**),[13] ozonolysis of the corresponding *N*-alkenyl triflouroacetic acid amides followed by a Wittig reaction with ethyl (triphenylphosphoranylidene)acetate and alkaline hydrolysis of the products yielded the amines (**21**, **22**).

2-Allylpyrrolidine (**23**) was obtained through lithiation of the *t*-Boc protected pyrrolidine, whose stabilized anion was substituted electrophilically with allyl bromide and finally hydrolysis using trifluoroacetic acid.[14]



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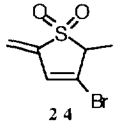

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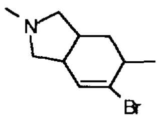
The outcome of the ring-opening reaction was found to be dependent on the base strength and on the nucleophilicity of the attacking amine. Steric factors do also affect the reaction as no ring-opening occured when using 2,2,6,6-tetramethylpiperidine alone. The action of the amine is dual, it works first as a base to tautomerize the thiophene-1,1-dioxide into an exocyclic diene (**24**), which is nucleophilically attacked, and ring-opened, by another amine molecule in a Michael addition like way; addition of amines to vinylic sulfones is known to work in a variety of solvents such as ether[15], acetonitrile[16] and aqueous ethanol[17], but here toluene worked best; a shift towards other components in the product was observed as the polarity of the solvent increased.

The non-cyclic amines **17**, **18** and **19** did react, but more sluggishly and in lower yields than piperidine, which can not solely be accounted for by the lowered temperatures. The reaction itself is complex and gives rise to a number of undesired components. When conducted in a sealed tube under argon at 100 °C for 24 hours, the reaction between **9** and **17** gave a 71 % GLC yield of 1-amino-4-bromo-*N*-methyl-*N*-(1-prop-2-enyl)-(2*E*, 4*Z*)-2,4-hexadiene (**25**) (31 %) together with two isomers (8 % and 9 %) and four other nitrogen containing components, amongst which was an intramolecular Diels-Alder product, 4-bromo-2,2a,6,6a,7-pentahydro-1,5-dimethylisoindole(**26**) (11 %), formed from **25** or possibly from an intermediary sulfolene such as **27**; one unidentified compound(6 %); one ring-opened, debrominated, doubly amino substituted product, 1,3-di-(*N*-methyl-*N*-prop-2-enylamino)-2,4-hexadiene (3 %, **28**), whose structure was inferred from its mass spectrum and through mechanistic considerations; and one none ring-opened product, 4-bromo-2,3-dihydro-2-*N*-methyl-*N*-(prop-2-enyl)-aminomethyl-thiophene-1,1-dioxide (11%, **29**), which could have been formed by an attack on an intermediate, **30**, the other two amines gave similar products under normal reaction conditions.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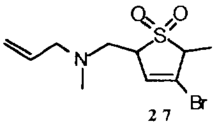
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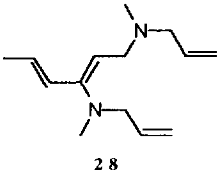
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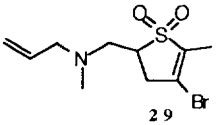
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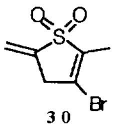
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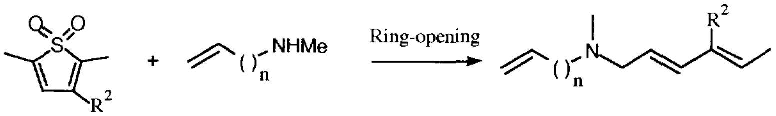
Neither of the amines **21** and **22** did ring-open any dioxides, not even when a tenfold excess of an assisting base such as TMEDA or 2,2,6,6-tetramethyliperidine was added, nor did **20** give more than trace amounts of the expected triene when reacting with **9**. It was therefore tempting to try an α-monosubstituted cyclic amine like **23**, as we previously have been succesful with pyrrolidine.[1] In this case the ring-opening also worked but also here three isomeric trienes were formed as in the case with acyclic amines along with the usual set of other compounds in a 57 % total yield.

Turning to the effects of substituents in the thiophene-1,1-dioxides, rather few of the substituted derivatives were suited for the ring-opening reaction. The model substance **9** worked best of all. In the reaction with **17**, **18** and **19** the following trienes were obtained 1-amino-4-bromo-*N*-methyl-*N*-(1-prop-2-pro-



R^2=Br,**9**
R^2=SiMe$_3$, **10**
R^2=H, **11**

n=1,2,3

R^2=Br, H
25,31,32,35,36

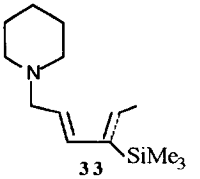
Scheme 3

Table 3. Isolated yields (%) of trienes (**25,31,32,35,36**)

thiophene-1,1-dioxide	amine	triene	isolated yield (%)
9	**17**	**25**	31
9	**18**	**31**	32
9	**19**	**32**	35
10	**18**	**35**	11
11	**17**	**36**	30

penyl-(*2E,4Z*)-2,4-hexadiene (**25**), 1-amino-4-bromo-N-(1-but-3-enyl)-*N*-methyl-(2*E*,4*Z*)-2,4-hexadiene (**31**) and 1-amino-4-bromo-*N*-methyl-N-(1-pent-4-enyl)-(2*E*,4*Z*)-2,4-hexadiene (**32**) in 31, 32 and 35 % yield respectively (Scheme 3, Table 3). The (*4Z*)-configuration was determined by measuring the coupling constant between H5 and C3, which was found to be 4.2 Hz for the three trienes, a (*4E*)-configuration would have given a coupling constant of about 8 Hz.[18] The (*2E*)-configuration, or the *trans* configuration, was determined through the characteristic 15 Hz coupling between H2 and H3.

Although **10**[2] and **15** do ring-open in their reaction with piperidine, giving **33**[2] and **34**, they fail to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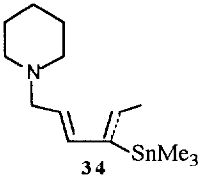
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give the corresponding substituted trienes when reacting with **17** and **18**, in part due to the extended reaction times required for these amines. According to GLC analysis comparing the peak areas of the two main products, the ring-opening seems to preceed the loss of the silyl and stannyl groups in both these cases. However, using either of the dioxides **10** or **15** together with **18** the desilylated respectively destannylated triene 1-amino-*N*-(1-but-3-enyl)-*N*-methyl-(*2E,4E*)-2,4-hexadiene(**35**) could be obtained in up to 30 % yield. Amino-*N*-methyl-*N*-(1-prop-2-enyl)-(*2E,4E*)-2,4-hexadiene (**36**) was synthesized in a sealed tube under argon **11** and **17** at 100 °C for 22 h in 11 % yield.Therefore, it seems to be a better synthetic route to go *via* the 3-silyl substituted dioxide rather than the parent 2,5-disubstituted thiophene-1,1-dioxide. The (*E,E*)-configuration of **35** and **36** was determined through the *trans* coupling constants of about 14 Hz.

Bulky substituents in position 5, as in **12** and **14**, made it virtually impossible to ring-open the dioxides, not even trace amounts of the trienes were formed. Compound **13** was defunctionalized as soon as the amine was added, and did not give any desired products when the reaction proceeded. In the attempts to ring-open **16** it is likely that it rapidly lost the silyl group, then was transformed into the keto form and as such decomposed completely as no sole product could be identified. Thus, the ring-opening worked satisfactory only for R^2 equal to bromo and trimethylsilyl, if total desilylation is acceptable.

Further investigations are under way dealing with the mechanism of the ring-opening reaction and the synthesis of alkaloid-like building blocks through an intramolecular Diels-Alder reaction of the trienes described in this paper.

EXPERIMENTAL

Chemicals and Instrumentation

The ^{1}H NMR and ^{13}C NMR spectra were recorded on a 300 MHz Varian XL-spectrometer using deuterochloroform as solvent.The mass spectra were recorded on a JEOL-SX 102 spectrometer and the IR spectra on a Perkin Elmer 298 infrared spectrophotometer. GLC analyses were carried out on a Varian 3300 gas chromatograph using an OV-17 (3 %) packed column. Melting points are uncorrected. Column chromatography was performed with Merck silica gel 60. All solvents were distilled and purified according to standard procedures prior to use. Purchased starting materials were used without further purification.

3-Bromo-2,5-dimethylthiophene **1**:

This compound was prepared according to Hörnfeldt *et al.*[9]

3-Trimethylsilyl-2,5-dimethylthiophene **2**:

This compound was prepared according to Gronowitz *et al.*[2]

2-Methyl-5-(tert-butyldimethylsilyl)thiophene **4**:

This compound was prepared following a method by Gronowitz *et al.*.[2] 2-Bromo-5-methylthiophene (3.54 g, 20.0 mmol) was dissolved in 20 ml of anhydrous diethyl ether at -70 °C under a nitrogen atmosphere and 18.5 ml 1.3 M (24.0 mmol) *sec*-butyllithium in pentane was added dropwise. After 2 h and 25 min, *tert*-butyldimethylsilyl chloride (3.62 g, 24.0 mmol) was added in one portion and the reaction mixture was slowly allowed to reach room temperature, whereafter it was washed with water, dried over magnesium sulfate, evaporated *in vacuo* and distilled under reduced pressure; b.p. 98-102 °C/13 mmHg. The title compound was obtained in a yield of 0.92 g (22%). ^{1}H NMR: δ 7.04 (d, 1H, H4, J = 3.2 Hz), 6.83 (m, 1 H, J = 3.2, 1.3 Hz), 2.51 (d, 3H, 2-CH$_3$, J = 1.3 Hz), 0.98 (s, 9 H, *t*-Bu), 0.29 (s, 6 H, Si(CH$_3$)$_2$). Peak match-ing for M$^+$. Calcd. for $C_{11}H_{20}SSi$: 212.1053. Found 212.1053.

3-Bromo-2-trimethylsilyl-5-methylthiophene **5**:

This compound was prepared analogous to **4** from 2,3-dibromo-5-methylthiophene[9] (10.2 g, 40.0 mmol), anhydrous diethyl ether 30 ml), butyllithium in cyclohexane (93 ml, 2M) and trimethylsilyl chloride (5.22 g, 48.0 mmol). Reaction time for halogen metal exchange was 1.5h and for silylation 2.0h. The title compound was obtained in a yield of 6.52 g (65 %), bp 107-110 °C/11 mm Hg.

3-Bromo-2-isopropenyl-5-methylthiophene :

This compound was prepared following a literature method.[7] To a solution of 2,3-dibromo-5-methylthiophene (16.9 g, 66.0 mmol) in 20 ml of anhydrous diethyl ether under a nitrogen atmosphere at -70 °C 33 ml 2.0 M butyllithium in cyclohexane was added dropwise. After 1.5 h, acetone(4.85 ml, 66.0 mmol) in 70 ml of anhydrous diethylether was added dropwise to the reaction mixture, which was stirred for another 1.3 h before it was allowed to reach room temperature. Then the reaction mixture was poured onto an slurry of ice and hydrochloric acid, the phases were separated and the water phase was extracted three times with ether and the combined ether phases were washed with water, dried over magnesium sulfate and evaporated *in vacuo*. The crude product was refluxed for 1.0 h with 0.5 g oxalic acid at 60 °C/11 mmHg. Distillation at reduced pressure under nitrogen afforded 8.94 g (62 %) of the title compound, b.p. 76-77°C/1.5 mmHg . ^{1}H NMR: δ 6.60 (q, 1H, H4, J = 1.1 Hz), 5.48 (m, 1H, *cis-i*Pr-CH, J = 0.9 Hz), 5.20 (m, 1H, *trans-i*Pr-CH, J = 1.5 Hz), 2.42 (d, 3H, 5-CH$_3$, J = 1.1 Hz), 2.16 (dd, 3H, *i*Pr-CH$_3$, J = 0.9, 1.5 Hz).

3-Bromo-2-isopropyl-5-methylthiophene **6**:

This compound was prepared following a literature method.[7] The compound described above (3.08 g, 14.19 mmol) and *tris*(triphenylphosphine)rodhium chloride (85.3mg, 97 µmol) were added to a mixture of toluene and heptane (3:1) in a flask, which subsequently was placed in a Parr hydrogenation apparatus and flushed three times with hydrogen. Complete hydrogenation was achieved after 18 h at a hydrogen pressure of 3.77 atm. After filtration the product was distilled at reduced pressure under nitrogen giving 2.22 g (71 %) of **5**; b.p. 94-96 °C/11 mmHg. ^{1}H NMR: δ 6.60 (q, 1H, H4, J = 1.2 Hz), 3.28 (sept, 1H, 2-CH, J = 6.9 Hz), 2.42(d, 3H, 5-CH$_3$, J = 1.2 Hz), 1.26 (d, 6H, 2-CH$_3$, J = 6.9 Hz) MS: m/z (%) 218/220 (M$^+$, 65), 203/205 (100), 139 (28), 124 (80), 77 (22), 59 (60).

3-Trimethylstannyl-2,5-dimethylthiophene **7**:

This compound was prepared according to Gronowitz *et al.*[2]

2,5-Dimethyl-3-triisopropylsiloxythiophene **8**:

This compound was prepared following a literature method.[10] A mixture of 2,5-dimethyl-3-hydroxythiophene[9] (407 mg, 3.17 mmol), triisopropylchlorosilane (734 mg, 3.81 mmol) and imidazole (540 mg, 7.93 mmol) in 1.0 ml of *N,N*-dimethylformamide was stirred for 5.5h at 45 °C. The reaction mixture was diluted with dichloromethane and washed three times with water; dried over magnesium sulfate and evaporated *in vacuo* to give a crude oil, which was chromatographed on 50 g silica using heptane as eluant. The title compound was obtained in a yield of 346 mg (38 %). ^{1}H NMR: δ 6.29 (q, 1H, H4, J = 2.0 Hz), 2.33 (d, 3H, 5-CH_3), 2.19 (s, 3H, 2-CH_3), 1.10 (d, 18H, *i*-Pr CH_3, J = 7.2 Hz), 0.91 (sept, 3H, *i*-Pr CH, J = 7.2 Hz).

Oxidation with methachloroperbenzoic acid, Procedure A.

This procedure is according to a literature method.[6] To a solution of *meta*-chloroperbenzoic acid (345 mg, 20 mmol) in dichloromethane (100 ml), the appropriate thiophene derivative(10 mmol) in dichloromethane (10 ml) was added dropwise at ambient temperature. For the silylated thiophenes the reverse order of addition was used in order to improve the yields. The work-up consisted of filtration and cooling the reaction mixture to -55 °C in order to remove the remaining *meta*-chloroperbenzoic acid by stirring the solution with amberlyst A-21. The ion exchange resin was removed and the solution evaporated. The residue so obtained was recrystallized from ethanol.

Oxidation with dimethyldioxirane, Procedure B.

This procedure was according to known methods.[8,19] 38 ml freshly distilled dioxirane/acetone solution (roughly 5 mol%, determined by comparing the dioxirane signals to the ^{13}C-satellites of acetone in the ^{1}H NMR spectrum), or the total yield from 100 g of oxone, was added in one portion to 0.70 mmol of the thiophene derivative in 10 ml dichloromethane at 5 °C. Completion of the reaction was achieved within 3 h. Evaporation *in vacuo* followed by recrystallation of the residue from ethanol yielded the dioxides.

3-Bromo-2,5-dimethylthiophene -1,1-dioxide **9**:

This compound was prepared according to procedure A.

3-Trimethylsilyl-2,5-dimethylthiophene-1,1-dioxide **10**:

This compound was prepared according to procedure A.

2,5-Dimethylthiophene-1,1-dioxide **11**:

This compound was prepared according to procedure A.

2-Methyl-5-(tert-butyldimethylsilyl)thiophene-1,1-dioxide **12**:

This compound was synthesized according to procedure A from **3** (0.92 g , 4.33 mmol) and after 16h 0.78 g (74 %) of **10** was obtained, mp 70-71 °C. ^{1}H NMR: δ 6.82 (dd, 1H, H4, J = 0.5, 4.1 Hz), 6.27 (m, 1H, H3, J = 4.1, 2.0 Hz), 2.12 (dd, 3H, 2-CH_3, J = 2.0 , 0.5 Hz), 0.97 (s, 9H, *t*-Bu), 0.29 (s, 6H, $Si(CH_3)_2$). Peak matching for M^+. Calcd for $C_{11}H_{20}O_2SSi$: 244.0953. Found 244.0953.

3-Bromo-5-methyl-2-trimethylsilylthiophene-1,1-dioxide **13**:

This compound was synthesized according to procedure A from **4** (3.37 g, 13.52 mmol) and after 68h 2.82 g (74 %) of **11** was obtained. ^{1}H NMR: δ 6.27 (q, 1H, H4, J = 1.9 Hz), 2.15 (d, 3H, 5-CH_3, J = 1.9 Hz), 0.43 (s, 9 H, $Si(CH_3)_3$. Peak matching for M^+. Calcd. for $C_8H_{13}O_2SSiBr$: 279.9589. Found 279.9590.

3-Bromo-2-isopropyl-5-methylthiophene-1,1-dioxide **14**:

This compound was synthesized according to procedure A from **5** (2.19 g, 10.0 mmol) and after 19h the oil obtained was subjected to HPLC workup on a polygosil silica column with heptane/ethyl acetate/2-propanol (90:9.9:0.1) as eluent. **12** was obtained as white crystals in a yield of 0.97 g (39 %) mp 68-70 °C. ^{1}H NMR: δ 6.26 (q, 1H, H4, J = 1.9 Hz), 3.11 (sept, 1H, 2-CH, J = 7.1 Hz), 2.11(d, 3H, 5-CH_3, J = 1.9 Hz), 1,40 (d, 6H, 2-CH_3, J = 7.1 Hz). MS: m/z (%)= 250/252 (M^+, 10), 186/188 (10), 171 (30), 107 (100), 91 (80). Peak matching for M^+. Calcd. for $C_8H_{11}O_2SBr$: 249.9663. Found 249.9665.

2,5-Dimethyl-3-trimethylstannylthiophene-1,1-dioxide **15**:

This compound was synthesized according to procedure B from **6** (317 mg, 1.15 mmol) and after 45 min 231 mg (65 %) of **13** was obtained, mp 98-100 °C. ^{1}H NMR: δ 6.28 (q, 1H, H4, J = 1.7 Hz), 2.08 (d, 3H, 5-CH_3, J = 1.7 Hz), 2.12 (s, 3H, 2-CH_3), 0.32 (s, 9 H, $Sn(CH_3)_3$. MS: m/z (%)= 308 (M^+, 5), 293 (15), 260 (55), 229 (100), 189 (55), 165 (77), 135 (30), 120 (10), 77 (15). Peak matching for M^+. Calcd. for $C_9H_{16}O_2SSn$: 307.9893. Found 307.9894.

2,5-Dimethyl-3-triisopropylsiloxythiophene-1,1-dioxide **16:**

This compound was synthesized according to procedure B from **7** (151 mg, 0.53 mmol) and after 2h and 40 min and work-up the residue upon evaporation was chromatographed on 7.5 g silica using heptane/ ethyl acetate (95:5) as eluent. **14** was obtained in a yield of 42 mg (25 %). ^{1}H NMR: δ 6.09 (q, 1H, H4, J = 1.9 Hz), 2.13 (d, 3H, 5-CH_3, J = 1.9 Hz), 1.93 (s, 3H, 2-CH_3), 0.9-1.10 (21 H, i-Pr). Peak matching for M^+. Calcd. for $C_{15}H_{28}O_3SSi$: 316.1529. Found 316.1532.

General procedure for reaction of amines with thiophene-1,1-dioxides:

This procedure was analogous to that of Gronowitz *et al.*[1] The dioxide (5.0 mmol) was dissolved in 15 ml toluene in a three-necked flask, equipped with a condenser, a septum and a thermometer. The reaction mixture was heated to temperatures depending on the amine. 60 °C for **17**, **20** and **21**, 80 °C for **18** and 100 °C for **19**, **22** and piperidine, the reference amine. The amines (20.0 mmol)were solved in 5.0 ml of toluene and then added dropwise *via* a syringe. The reactions were followed both by TLC and GLC.

When the starting material was consumed the triene amines were extraction with 1 % hydrochloric acid, the combined water phases were neutralized with 2 M sodium hydroxide solution. The product was extracted three times with diethyl ether, the ether phases were dried over magnesium sulfate and then evaporated. The residue, a brownish oil, was subsequently subjected to HPLC using a semi preparative nucleosil silica column (500x10) and heptane/ethyl acetate/triethyl amine (60:35:5) as eluant.

1- Amino-4-bromo-N-methyl-N-(1-prop-2-enyl)-(2E,4Z)-2,4-hexadiene **25**:

This compound was prepared as described above from **9** (1.12g, 5.00 mmol) and **17** (360 mg, 2.29 mmol) and after 22h 1.42 g (31 %) of **25** was obtained. IR (cm^{-1}): ν 1640 (s, C=C-stretch, conjug. diene), 1615 (m, C=C-stretch, RCH=CH_2), 990 (s, CH-bend, RCH=CH_2), 920 (s, CH-bend, RCH=CH_2), 950 (s, CH-bend, trans-RCH=CHR), 820 (m, CH-bend, R_2C=CHR). ^{1}H NMR: δ 6.15 (d, 1H, 3-CH, J = 14.9 Hz), 6.08 (dt, 1H, 2-CH, J = 6.4 Hz, 14.9 Hz), 5.98 (q, 1H, 5-CH, J = 6.7 Hz), 5.87 (m, 1H, N-2-CH, J = 17.1, 6.4 Hz), 5.21 (m, 1H, N-3-CH-cis, J = 17.1, 1.5 Hz), 5.16 (m, 1H, N-3-CH-trans, J = 1.5 Hz), 3.10 (d, 2H, 1-CH_2, J = 6.4 Hz), 3.01 (d, 2H, N-1-CH_2, J = 6.4 Hz), 2.21 (s, 3H, N-CH_3), 1.87 (d, 3H, 6-CH_3, J = 6.8 Hz). ^{13}C NMR: δ 135.65 (N-2-CH), 131.69 (3-CH), 130.67 (2-CH), 128.19 (5-CH), 126.02 (4-CH), 117.64 (N-3-CH_2), 60.61 (1-CH_2), 58.50 (N-1-CH_2), 42.10 (N-CH_3), 17.19 (6-CH_3). MS: m/z (%)= 229/231 (M^+, 5), 214/216 (7), 150 (100), 108 (62), 79 (57), 42 (43). Peak matching for M^+. Calcd. for $C_{10}H_{16}NBr$: 229.0466. Found 229.0472.

4-Bromo-2,2a,6,6a,7-pentahydro-1,5-dimethylisoindole **26**:

^{1}H NMR: δ 6.07 (dd, 1H), 3.01 (dd, 1H), 2.80 (d, 1H), 2.72 (m, 1H,) 2.43 (m, 1H), 2.38 (m, 1H), 2.34 (s, 3H), 2.28 (d, 1H), 2.16 (dd, 1H), 1.89 (dt, 1H), 1.40 (m, 1H), 1.17 (d, 3H). ^{13}C NMR: δ 131.00, 129.73, 62.71, 60.38, 42.39, 41.74, 37.96, 35.87, 35.61, 21.76. MS: m/z (%)= 229 (M^+, 10), 150 (80), 107 (60), 91 (25), 57 (100), 42 (33). Peak matching for M^+: Calcd. for $C_{10}H_{16}NBr$: 229.0466. Found 229.0466.

4-Bromo-2,3-dihydro-2-N-methyl-N-(prop-2-enyl)-aminomethyl-thiophene-1,1-dioxide **27**:

^{1}H NMR: δ 5.85 (m, 1H), 5.20 (m, 1H), 5.17 (m, 1H), 3.58 (m, 1H), 3.16 (m, 1H), 3.08 (m, 2H), 2.95 (m, 2H), 2.66 (dd, 1H), 2.29 (s, 3H), 2.03 (t,3H). ^{13}C NMR: δ 138.23, 134.86, 128.90, 118.90, 61.08, 57.88, 54.65, 42.37, 38.72, 9.48. MS: m/z (%): 293/295 (M^+, 5), 214 (10), 150 (58), 84 (100), 70 (60), 41 (36).

1-Amino-4-bromo-N-(1-but-3-enyl)-N-methyl-(2E,4Z)-2,4-hexadiene **31:**

This compound was prepared as described above from **9** (1.12 g, 5.00 mmol) and **18** (1.68 g, 20.0 mmol). After 19h 390 mg (32 %) of the triene **31**was obtained. IR(cm^{-1}): ν 1640 (s, C=C-stretch, conjug. diene), 1615 (m, C=C-stretch, $RCH=CH_2$), 990 (s, CH-bend, $RCH=CH_2$), 920 (s, CH-bend, $RCH=CH_2$), 950 (s, CH-bend, trans-RCH=CHR), 820 (m, CH-bend, $R_2C=CHR$). ^1H NMR: δ 6.17 (d, 1 H, 3-CH, J = 14.9 Hz), 6.04 (dt, 1H, 2-CH, J = 6.35, 14.9 Hz), 5.97 (q, 1H, 5-CH, J = 6.6 Hz), 5.80 (m, 1H, N-3-CH, J = 18.0, 6.7 Hz), 5.09 (m, 1H, N-4-CH-cis, J = 18.0 Hz), 5.03 (m, 1H, N-4-CH-*trans*), 3.11 (d, 2H, 1-CH_2, J = 6.4 Hz), 2.43 (t, 2H, *N*-1-CH_2, J = 7.5 Hz), 2.27 (m, 2H, *N*-2-CH_2, J = 7.5 , 6.7 Hz), 2.23 (s, 3H, *N*-CH_3), 1.87 (d, 3H, 6-CH_3, J = 6.6 Hz). ^{13}C NMR: δ 136.67 (*N*-3-CH), 131.54 (3-CH), 130.74 (2-CH), 128.12 (5-CH), 126.05(4-CH), 115.60 (*N*-4-CH_2), 59.06 (1-CH_2), 56.72 (N-1-CH_2), 42.10 (N-CH_3), 31.94 (*N*-2-CH_2), 17.18(6-CH_3). MS: m/z (%)= 243/245 (M^+, 5), 202/205 (100), 159/161 (70), 122(10), 98 (6), 80 (92), 44 (37). Calcd. for $C_{11}H_{18}NBr$: 243.0602. Found 243.0602.

1-Amino-4-bromo-N-methyl-N-(1-pent-4-enyl)-(2E,4Z)-2,4-hexadiene **32:**

This compound was prepared as described above from **9** (3.71 g, 16.6 mmol) and **19** (6.60 g, 66.6 mmol). After 5.25h 1.52 g (35 %) of the triene **32** was obtained. IR (cm^{-1}): ν 1640 (s, C=C-stretch, conjug. diene), 1615 (m, C=C-stretch, $RCH=CH_2$), 990 (s, CH-bend, $RCH=CH_2$), 920 (s, CH-bend, $RCH=CH_2$), 950 (s, CH-bend, trans-RCH=CHR), 820 (m, CH-bend, $R_2C=CHR$). ^1H NMR: δ 6.13 (d, 1H, 3-CH, J = 14.8 Hz), 6.06 (dt, 1H, 2-CH, J = 6.4 , 14.8 Hz), 5.97 (q, 1H, 5-CH, J= 6.8 Hz), 5.81 (m, 1H, *N*-4-CH, J= 16.9, 6.7 Hz), 5.04 (m, 1H, *N*-5-CH-*cis*, J = 16.9 Hz), 4.93 (m, 1H, 5-CH-*trans*), 3.01 (d, 2H, 1-CH_2, J = 6.4 Hz), 2.34 (t, 2H, *N*-1-CH_2, J = 7.6 Hz), 2.20 (s, 3H, *N*-CH_3), 2.05 (m, 2H, *N*-3-CH_2, J = 7.9, 6.7 Hz), 1.86 (d, 3H, 6-CH_3, J = 6.8 Hz), 1.56 (m, 2H, *N*-2-CH_2, J = 7.8, 7.9 Hz). ^{13}C NMR: δ 138.5 (*N*-4-CH), 131.4 (3-CH), 131.0 (2-CH), 128.0 (5-CH), 126.1 (4-CH), 114.6 (N-5-CH_2), 59.2 (1-CH_2), 56.9 (*N*-1-CH_2, 42.2(*N*-CH_3), 31.6(*N*-3-CH_2), 26.7(*N*-2-CH_2), 17.2 (6-CH_3). MS: m/z (%)= 257/259 (M^+, 10), 216/218 (7), 202/204 (37), 178 (100), 159/161 (78), 79 (95), 42 (37). Peak matching for M^+. Calcd. for $C_{12}H_{20}NBr$: 257.0779/ 259.0759. Found 257.0770/ 259.0752.

1-(1-Piperidino)-4-trimethylstannyl-(2E,4Z)-2,4-hexadiene **34**:

This compound was obtained according to the general procedure from **9** (94.0 mg, 0.31 mmol) and piperidine (200 mg, 2.35 mmol). The reaction time was 4h and as eluent for HPLC heptane/ethyl acetate/triethyl amine (75:22.5:2.5) was used. Two components were separated, 15.2 mg (30 %) of the destannylated diene and 17.7 mg (15 %) of diene **34** . ^1H NMR: δ 6.25 (d, 1H, 3-CH, J = 13.5 Hz), 6.21 (m, 1H, 2-CH, J = 6.78, 13.5 Hz), 5.60 (q, 1H, 5-CH, J = 5.8 Hz), 3.02 (d, 2H, 1-CH_2, J = 6.8 Hz), 2.37 (b, 4 H, *N*-$(CH_2)_2$), 1.73 (d, 3H, 6-CH_3, J = 5.8 Hz), 1.58 (b, 4 H, *N*-$(CH_2CH_2)_2$), 1.43 (b, 2 H, *N*-$CH_2CH_2CH_2$), 0.25 (s, 9 H, $Sn(CH3)_3$). MS: m/z (%)= 329 (M^+, 4), 314 (82), 164 (100), 151 (12), 135 (10), 98 (100), 84 (40).

1-Amino-N-(1-but-3-enyl)-N-methyl-(2E,4E)-2,4-hexadiene **35**:

This compound was prepared according to the general procedure from **10** (209 mg, 0.97 mmol) and **18** (330 mg, 3.90 mmol). The reaction time was 46h and the desilylated triene **35** was obtained in a yield of 47.4 mg (30 %). ^1H NMR: δ 6.10 (m, 1H, 3-CH, J = 14.5, 10.4 Hz), 6.08 (m, 1H, 4-CH, J = 10.4, 14.5 Hz), 5.79 (m, 1H, *N*-3-CH, J = 6.7, 17.1 Hz), 5.66 (m, 1H, 5-CH, J= 14.4, 6.6 Hz), 5.55 (m, 1 H, 2-CH, J = 6.8, 14.5 Hz), 5.06 (m, 1H, *N*-4-CH-*cis*, J = 17.1 Hz), 5.00 (m, 1H, *N*-4-CH-*trans*, J = 10.2 Hz), 3.02 (d, 2H, 1-CH_2, J = 6.8 Hz), 2.52 (t, 2H, *N*-1-CH_2, J = 6.6 Hz), d= 2.23 (m, 2 H, N-2-CH_2, $J_{N-1-CH2}$= 6.6

Hz, $J_{N\text{-}3\text{-}CH}$= 6.7 Hz), d= 2.22 (s, 3 H, N-CH_3), d= 1.75 (d, 3 H, 6-CH_3, $J_{5\text{-}CH}$= 6.6 Hz).^{13}C NMR: d= 136.72(N-3-CH), 133.16(3-CH), 131.13(2-CH), 128.73(5-CH), 127.94(4-CH), 115.53(N-4-CH_2), 59.85(1-CH_2), 56.55(N-1-CH_2), 41.98(N-CH_3), 31.88(N-2-CH_2), 18.03(6-CH_3).
HRMS: found 165.1509; calculated for $C_{11}H_{19}N$: 165.1518. IR(cm^{-1}): 1640 (s, C=C-stretch, conjug. diene), 990 (s, CH-bend, RCH=CH_2), 910 (s, CH-bend, RCH=CH_2).

1-Amino-N-methyl-N-(1-prop-2-enyl)-(2E,4E)-2,4-hexadiene **36:**

A 50 ml glass ampoule was charged with 2,5-dimethylthiophene-1,1-dioxide (**11**) (83.6 mg, 0.58 mmol), **17** (330 mg, 4.64 mmol) and toluene (5 ml). The ampoule was then evacuated and flushed with argon before it was sealed and placed in a steel bomb in an oven at 100 °C for 70 hours. The reaction mixture was worked up according to the general procedure and gave 9.85 mg (11%) of **36**. IR (cm^{-1}): ν 1640 (s, C=C-stretch, conjug. diene), 990 (s, CH-bend, RCH=CH_2), 920 (s, CH-bend, RCH=CH_2). ^{1}H NMR: δ 6.10 (m, 1H, 3-CH, J = 14.5, 10.4 Hz), 6.07 (m, 1H, 4-CH, J = 10.4, 14.3 Hz), 5.86 (m, 1H, *N*-2-CH, J = 6.7, 16.9, 10.3 Hz), 5.65 (m, 1H, 5-CH, J = 14.3, 6.7 Hz), 5.57 (m, 1H, 2-CH, J = 6.8,14.5 Hz), 5.16 (m, 1H, *N*-3-CH-*cis*, J = 16.9 Hz), 5.13 (m, 1H, *N*-3-CH-*trans*, J = 10.2 Hz), 3.00 (d, 2H, 1-CH_2, J = 6.8 Hz), 2.98 (d, 2H, *N*-1-CH_2, J = 6.7 Hz), 2.18 (s, 3H, *N*-CH_3), 1.74 (d, 3H, 6-CH_3, J = 6.7 Hz). ^{13}C NMR: δ 135.7 (*N*-3-CH), 133.3 (3-CH), 131.1 (2-CH), 128.8 (5-CH), 127.9 (4-CH), 117.6 (*N*-4-CH_2), 60.4 (1-CH_2), 59.4 (*N*-1-CH_2), 41.9 (*N*-CH_3), 18.0 (6-CH_3). Peak matching for M^+. Calcd. for $C_{10}H_{17}N$: 151.1361. Found 151.1368.

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