Intramolecular Diels–Alder Reactions of 1-Thia-3-azabutadienes. One-Pot Synthesis of Annulated Thiazines from *N*-(Trimethylsilyl)imines and Isothiocyanates

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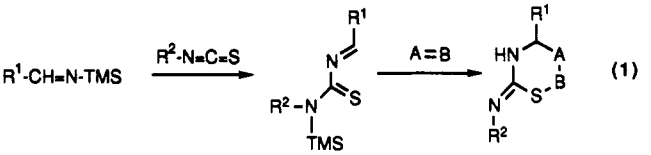
The intramolecular [4 + 2] cycloaddition of 1-thia-3-aza dienes is described. Substituted *N*-(trimethylsilyl)imines **2** derived from aromatic and heteroaromatic aldehydes **1** react with isothiocyanates to form heterodienes **3**, which, although not isolated, undergo intramolecular cycloaddition at 90 °C to yield heteropolycyclic compounds **5** and **7**. The process was found to be regioselective and stereospecific; the stereochemistry of the cycloadducts arises from an exo transition state.

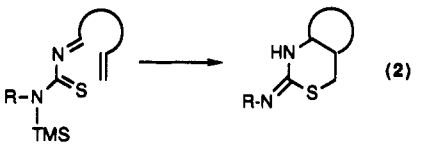
The Diels–Alder reaction is one of the most versatile methods for the synthesis of heterocyclic six-membered rings.[1] Cycloadditions with either heterodienophiles[2] or heterodienes,[3] or both, can be effected. On the other hand, the intramolecular Diels–Alder reaction has become a powerful tool for constructing complex polycyclic molecules in a regio- and stereoselective manner.[4] In this context, a great deal of attention has been paid in the last years to the intramolecular hetero-Diels–Alder reaction as a useful entry to polyheterocyclic compounds. Thus, in the last decade simple 1-azadienes[5] and 2-azadienes[6] as well as heteroazadienes, e.g., 1,2-diaza,[7] 1-oxa-2-aza,[8] and 1-oxa-3-aza dienes,[3a,9] have been shown to participate in this concerted process. However, intramolecular [4 + 2] cycloadditions involving 1-thia-3-aza dienes have not been reported as yet.[10]

In previous papers, we have reported on the synthesis[11] and intermolecular [4 + 2] cycloaddition reactions[12] of 1-thia-3-aza dienes. We have found that these heterodienes are able to cycloadd to a variety of electron-poor carbo- and heterodienophiles (e.g., acetylene and ethylene esters, *N*-phenylmaleimide, azo derivatives, etc.) under mild reaction conditions (eq 1).



(1)

Continuing our study on the reactivity of these systems as heterodienes, we now report that substituted 2-amino-1-thia-3-aza dienes having an unsaturated appendage at C-4, readily available from *N*-(trimethylsilyl)imines and isothiocyanates, undergo intramolecular Diels–Alder cyclization under mild reaction conditions (eq 2).[13]



(2)

Results and Discussion

Preparation of *N*-(Trimethylsilyl)imines 2a–f. The synthesis of *N*-(trimethylsilyl)imines **2a–f** was readily accomplished in very high yield from the corresponding aldehydes **1** and LHMDS following the procedure developed by Hart et al.[14] (see Experimental Section). The *N*-(trimethylsilyl)imines prepared as well as the yields obtained are collected in Table I.

In the case of compound **2d**, a 80:20 mixture of *E*/*Z* aldehyde, prepared from salicylaldehyde and commercial 4-bromo-2-butene (*E*/*Z* = 80/20), was used. The cinnamyl silylimines **2b** and **2c** were not isolated, but ether was added to the reaction mixture, lithium chloride filtered off, and the resulting solution used in the next step (see Experimental Section).

Intramolecular [4 + 2] Cycloaddition of 1-Thia-3-aza Dienes. The *N*-(trimethylsilyl)imines thus prepared were then allowed to react with aromatic and aliphatic isothiocyanates. Thus, heating a toluene solution of benzylidene amines **2a–d** (R¹ = H) and isothiocyanate at 90 °C for 10 h led, after aqueous workup, to adducts **5a–i** (60–88% yield) resulting from cycloaddition of the initially formed 1-thia-3-aza dienes **3** (Scheme I, Table II).[15] Cy-

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(2) Weinreb, S. M.; Staib, R. R. *Tetrahedron* **1982**, *38*, 3087.
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(8) Denmark, S. E.; Dappen, M. S.; Sternberg, J. A. *J. Org. Chem.* **1984**, *49*, 798; *Ibid.* **1984**, *49*, 4741.
(9) Melnick, M. J.; Weinreb, S. M. *J. Org. Chem.* **1988**, *53*, 850.
(10) For isolated examples of intermolecular [4 + 2] cycloadditions of 1-thia-3-azadienes, see: (a) Giordano, C.; Belli, A.; Abis, L. *Tetrahedron Lett.* **1979**, 1537. (b) Gokou, C. T.; Pradère, J.-P.; Quiniou, H. *J. Org. Chem.* **1985**, *50*, 1545. (c) Burger, K.; Goth, H. *Angew. Chem., Int. Ed. Engl.* **1980**, 810. (d) Burger, K.; Huber, E.; Schöntag, W.; Ottlinger, R. *J. Chem. Soc., Chem. Commun.* **1983**, 945. (e) Bakasse, M.; Reliquet, A.; Reliquet, F.; Duguay, G.; Quiniou, H. *J. Org. Chem.* **1989**, *54*, 2889.
(11) Barluenga, J.; Tomás, M.; Ballesteros, A.; López, L. A. *Synthesis* **1989**, 228.
(12) Barluenga, J.; Tomás, M.; Ballesteros, A.; López, L. A. *Tetrahedron Lett.* **1989**, 6923.
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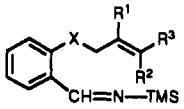
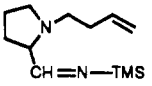
Table I. Synthesis of *N*-(Trimethylsilyl)imines 2 from Aldehydes 1

$$\underset{1}{ArCHO} \xrightarrow{LHMDS} \underset{2}{ArCH{=}NTMS}$$

compd	X	R^1	R^2	R^3	yield[a] (%)
					
2a	O	H	H	H	90
2b	O	H	H	Ph	[b]
2c	CH_2	H	H	Ph	[b]
2d	O	H	H, (Me)	Me, (H)	80[c]
2e	O	Me	H	H	88
					
2f					90

[a] Isolated yield. [b] Not isolated (see Experimental Section). [c] Isolated as a 80:20 mixture of *E* and *Z* diastereoisomers.

Table II. Cycloadducts 5a–i, 6a,b, and 7 from Silylimines 2a–d and 2f

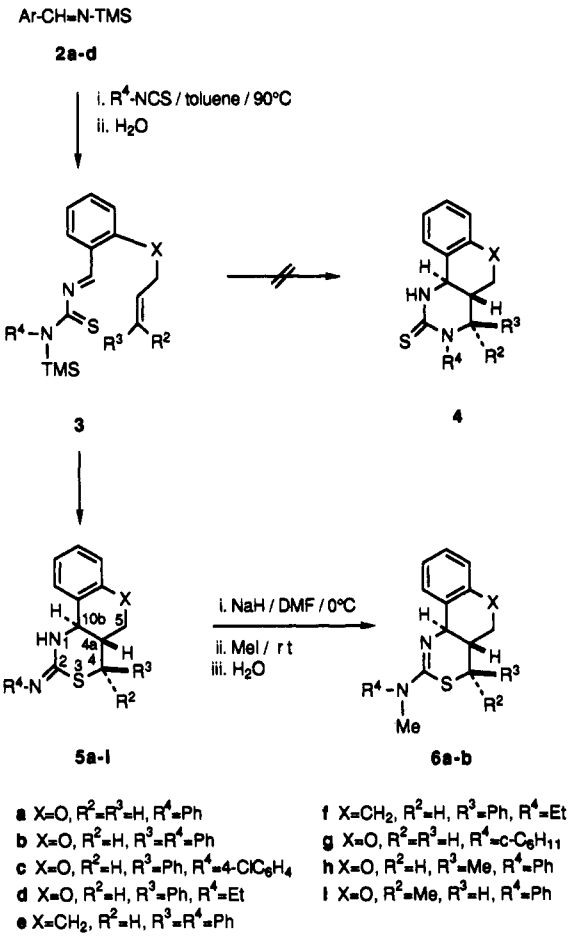
compd	X	R^2	R^3	R^4	yield[a] (%)	mp (°C)
5a	O	H	H	Ph	88	oil
5b	O	H	Ph	Ph	84	160–161[b]
5c	O	H	Ph	4-ClC_6H_4	88	209–210[b]
5d	O	H	Ph	Et	81	oil
5e	CH_2	H	Ph	Ph	70	oil
5f	CH_2	H	Ph	Et	60	oil
5g	O	H	H	c-C_6H_{11}	81	oil
5h	O	H	Me	Ph	80[c]	oil
5i	O	Me	H	Ph		
6a	O	H	H	Ph	90	143–145[b]
6b	O	H	Ph	Ph	92	196–197[b]
7					70	oil

[a] Yield after purification. [b] Recrystallized from *n*-hexane–chloroform. [c] 80:20 mixture of **5h**:**5i**.

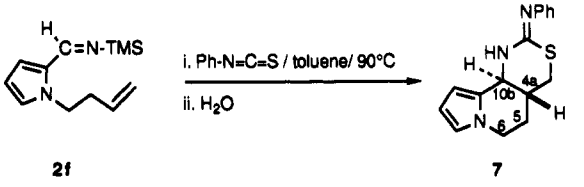
cloadducts **4**, which would arise from the participation of the 1,3-diazadiene tautomer as the 4π-component,[16] were ruled out on the basis of the ^{13}C NMR data. Thus, whereas the thione group resonates around 180 ppm in related heterocycles,[11,17,18] no signals were found in this case above 154 ppm. On the other hand, compounds derived from aromatic isothiocyanates (**5a–c**, **5e**, **5h–i**) exist in solution as the exo imino tautomers as evidenced from the shielding observed in the ^{13}C NMR spectra for the ortho (119–121 ppm) and para (122–125 ppm) carbon atoms of the *N*-aryl substituent R^4;[19,20] in contrast, these carbon atoms appear at 128–130 ppm in the methylarylamino structure **6a,b**,[19] prepared by methylation of the corresponding sodium salt of **5a** and **5b**, respectively (Scheme I).

The reaction proved to be totally regio- and stereoselective, since no other isomers were detectable in the crude mixture (^1H NMR, 300 MHz); moreover, the large coupling

Scheme I



Scheme II



constants (9.7–11.3 Hz) between H_{4a} and H_{10b} found in the ^1H NMR spectra in all instances clearly reveals that the trans-fused stereoisomers **5**,[21] arising from an exo transition state,[22] were actually the adducts formed in the reaction.

Furthermore, we found that the stereochemistry of the dienophile was always retained in the cycloaddition process. Thus, the ^1H NMR data of the cycloadducts **5b–f** (R^2 = H, R^3 = Ph), obtained from *trans*-cinnamyl silylimines **2b** and **2c**, are in agreement with an axial orienation—trans,trans arrangement—for H_4, H_{4a}, and H_{10b}; for instance, the ^1H NMR spectrum of **5c** shows the H_{10b} and H_4 hydrogens as two sets of doublets (J (H_4–H_{4a}) = 11.3 Hz; J (H_{10b}–H_{4a}) = 11.2 Hz) at 4.3 and 4.6 ppm, respectively.

Next, we used the (trimethylsilyl)imine **2d**, as a 80:20 mixture of *E*/*Z* isomers (R^2 = H, R^3 = Me and R^2 = Me, R^3 = H), in order to get evidence for the stereospecificity of the cycloaddition. Therefore, **2d** was treated with phenyl isothiocyanate under the above reaction conditions

(15) Heterodienes of this type were synthesized and isolated in the intermolecular case by heating a mixture of silylimine and isothiocyanate at 60 °C (ref 11). In the present reaction we have not attempted to isolate the dienes **3** since heating the mixture at the temperature required for the cycloaddition reaction (90 °C) greatly simplifies the process.

(16) This behavior of **3** has been found in the intermolecular cycloaddition to isocyanates (ref 11) and enamines (ref 17).

(17) Barluenga, J.; Tomás, M.; Ballesteros, A.; López, L. A. *Tetrahedron Lett.* **1989**, 4573.

(18) Singh, H.; Singh, P. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1013.

(19) Jackman, L. M.; Ten, T. *J. Am. Chem. Soc.* **1975**, *97*, 2811.

(20) We also assume the exo imino tautomer to be present in the case of adducts derived from aliphatic isothiocyanates (**5d** and **5f,g**) as the same NMR patterns are observed.

(21) Silverstein, R. M.; Bassler, G. B.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*; Wiley: New York, 1981.

(22) Throughout this work the terms exo/endo refer to the orientation of the dienophile-to-aryl connecting side chain, rather than R^2 or R^3 groups, with respect to the diene function.

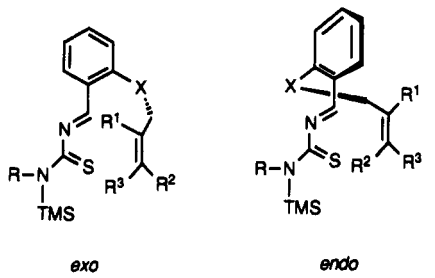


Figure 1.

giving rise to a mixture of diastereoisomers **5h** (R^2 = H, R^3 = Me) and **5i** (R^2 = Me, R^3 = H) in an approximate ratio of 80:20, according to ^1H and ^{13}C NMR (300 and 75 MHz, respectively) of the crude reaction mixture. The stereochemistry of both isomers **5h** and **5i**, which could not be separated, was ascertained on the basis of the coupling constants of the H_4 hydrogen.[23] Thus, in the case of the major diastereoisomer **5h**, derived from the *trans*-crotyl silylimine isomer **2d**, the H_4 resonates at 3.4 ppm as a doublet of quartet (J_1 (H_4–H_{4a}) = 10.4 Hz; J_2 (H_4–CH_3) = 6.6 Hz), while the H_4 hydrogen of the minor diastereoisomer **5i** is observed at 3.6 ppm as a quartet of doublet (J_1 (H_4–CH_3) = 6.9 Hz; J_2 (H_4–H_{4a}) = 4.7 Hz)). Furthermore, nuclear Overhauser enhancement experiments on the mixture clearly established the cis relationship of H_4 and H_{10b} in the major isomer **5h**.

The reaction also proved to be applicable to heterocyclic systems (Scheme II). Thus, imine **2f** derived from *N*-but-3-enylpyrrole-2-carbaldehyde was mixed with phenyl isothiocyanate in toluene and the reaction mixture heated at 90 °C for 10 h; then, aqueous workup and column chromatography afforded again the trans-fused cycloadduct **7** (J (H_{4a}–H_{10b}) = 9.7 Hz) in 70% yield (Table II).

It is worth noting that the cycloaddition was found to be fully stereoselective, with only a single stereoisomer being formed in all instances. Moreover, starting with the *E*/*Z* mixture **2d** we found the process to be stereospecific. The trans-fused stereoisomer obtained arises from an exo transition state, which is favored over the alternative endo counterpart (Figure 1). This preference appears to result from arene–heterodiene conjugation, which is maintained to a greater extent in the exo compared to the endo transition state.[24] In fact, the cyclization of the substituted imine **2e** (R^1 = Me) failed even under more drastic reaction conditions (toluene, 120 °C, 48 h) probably as a consequence of steric interaction between the methyl group of the dienophile and the nitrogen lone pair of the heterodiene.[25]

Conclusions

This work describes the first intramolecular hetero-Diels–Alder cycloadditions of 1-thia-3-azabutadienes with simple alkenes. The reaction takes place under very mild conditions involving exclusively an exo transition state to furnish stereoselectively trans-fused cycloadducts in good to excellent yields. This process allows the preparation of several structurally complex heterocyclic systems (benzopyranothiazines, naphthothiazines, and indolizinothiazines) in a single step from starting materials as readily available as *N*-(trimethylsilyl)imines and isothiocyanates.

Experimental Section

General Methods. Mp and bp are uncorrected. Spectroscopic instrumentation used has been described.[26] Column chromatography was performed with E. Merck silica gel (230–400 mesh) by standard flash chromatographic techniques.[27]

Materials. All reactions were run under a nitrogen atmosphere. All organic extracts were dried over anhydrous sodium sulfate. Toluene and THF were distilled from sodium benzophenone ketyl under nitrogen prior to use. 1,1,1,3,3,3-Hexamethyldisilazane and DMF were distilled from calcium hydride immediately before use. Aldehydes **1a,b** and **1d–f**, required for the preparation of (trimethylsilyl)imines **2a–b** and **2d–f**, were prepared by reaction of the sodium salt of salicylaldehyde or pyrrole-2-carbaldehyde with the appropriate alkyl halide. Aldehyde **1c** was prepared as described by Mariano et al.[6b] All other reagents were commercially available and were used as received.

Synthesis of *N*-(Trimethylsilyl)imines 2a–f (General Procedure). To 1,1,1,3,3,3-hexamethyldisilazane (4.6 mL, 22 mM) was added *n*-BuLi (8.0 mL, 2.5 M in hexane, 20 mM) over a 5-min period. The solution was stirred for 15 min, then cooled to 0 °C, and THF (35 mL) was added. After the solution was stirred for a further 20 min, the appropriate aldehyde (20 mM) in THF (5 mL) was added over 7 min. The resulting solution was stirred for 30 min at 0 °C and trimethylsilyl chloride (2.54 mL, 20 mM) was added in one portion. After stirring for 30 min, the solvents were removed in vacuo and the resulting *N*-(trimethylsilyl)aldimine distilled or used without purification (see below).

N-(Trimethylsilyl)imines **2a** and **2d–f** were prepared following this general procedure (reaction yields are given in Table I). Imines **2b** and **2c**, derived from cinnamaldehyde, were not distilled, but ether (30 mL) was added and lithium chloride filtered off. After the solvent was removed, the resulting (trimethylsilyl)imine was dissolved in toluene and used in the next step.

***N*-(Trimethylsilyl)-2-(1-oxabut-3-enyl)benzylideneamine (2a):** bp 115–119 °C (0.05 mmHg); IR (neat) 1640, 1600, 1240 cm^{-1}; ^1H NMR δ 0.1 (s, 9 H), 4.4 (d, J = 4.5 Hz, 2 H), 5.1 (dd, J = 10.4, 1.5 Hz, 1 H), 5.25 (dd, J = 17.3, 1.5 Hz, 1 H), 6.25 (m, 1 H), 6.7 (d, J = 7.5 Hz, 1 H, Ar), 6.8 (t, J = 7.5 Hz, 1 H, Ar), 7.1 (m, 1 H, Ar), 7.8 (dd, J = 7.5, 1.8 Hz, 1 H, Ar), and 9.3 (s, 1 H); ^{13}C NMR δ 164.8 (d), 158.7 (s), 132.9 (d), 132.2 (d), 126.9 (s), 126.8 (d), 120.7 (d), 117.0 (t), 112.2 (d), 66.8 (t), and −1.2 (q).

(*Z*,*E*)-*N*-(Trimethylsilyl)-2-(1-oxapent-3-enyl)-benzylideneamine (2d). Compound **2d** consisted of a 80:20 mixture of *E*/*Z* diastereoisomers that could not be separated, bp 122–125 °C (0.05 mmHg) (IR (neat) 1650, 1600, 1250 cm^{-1}). Compound (*E*)-**2d** (major isomer): ^1H NMR δ 0.2 (s, 9 H), 1.6 (d, J = 7.2 Hz, 3 H), 4.4 (d, J = 5.5 Hz, 2 H), 5.65 (m, 1 H), 5.75 (m, 1 H), 6.75 (d, J = 7.3 Hz, 1 H, Ar) 6.85 (t, J = 7.5 Hz, 1 H, Ar), 7.25 (td, J = 6.6, 2.0 Hz, 1 H, Ar), 7.9 (d, J = 7.6 Hz, 1 H, Ar), and 9.4 (s, 1 H); ^{13}C NMR δ 164.8 (d), 158.8 (s), 132.1 (d), 129.5 (d), 127.3 (s), 126.8 (d), 125.7 (d), 120.5 (d), 112.4 (d), 68.8 (t), 17.5 (q), and −1.3 (q). Selected NMR signals for compound (*Z*)-**2d** (minor isomer): ^1H NMR δ 4.55 (d, J = 3.6 Hz, CH_2); ^{13}C NMR δ 64.1 (t), 13.1 (q), and 1.7 (q).

***N*-(Trimethylsilyl)-2-(3-methyl-1-oxabut-3-enyl)-benzylideneamine (2e):** bp 118–122 °C (0.05 mmHg); IR (neat) 1640, 1620, 1230 cm^{-1}; ^1H NMR δ 0.1 (s, 9 H), 1.7 (s, 3 H), 4.3 (s, 2 H), 4.8 (s, 1 H), 4.9 (s, 1 H), 6.7 (m, 2 H, Ar), 7.2 (t, J = 7.6 Hz, 1 H, Ar), 7.8 (d, J = 7.6 Hz, 1 H, Ar), and 9.3 (s, 1 H); ^{13}C NMR δ 165.0 (d), 158.9 (s), 140.5 (s), 132.3 (d), 127.9 (s), 126.8 (d), 120.8 (d), 112.4 (d), 112.3 (t), 71.8 (t), 19.3 (q), and −1.2 (q).

***N*-(Trimethylsilyl)-1-(*N*-but-3-enylpyrrol-2-yl)-methyleneamine (2f):** bp 92–95 °C (0.05 mmHg); IR (neat) 1660, 1610, 1240 cm^{-1}; ^1H NMR δ 0.25 (s, 9 H), 2.5 (q, J = 7.0 Hz, 2 H), 4.5 (t, J = 7.0 Hz, 2 H), 5.1 (m, 2 H), 5.8 (m, 1 H), 6.2 (m, 1 H), 6.6 (m, 1 H), 6.8 (m, 1 H), and 8.9 (s, 1 H); ^{13}C NMR δ 158.0 (d), 135.0 (d) 132.2 (s), 127.8 (d), 118.9 (d), 116.5 (t), 107.8 (d), 48.1 (t), 35.8 (t), and −1.2 (q).

Preparation of Cycloadducts 5a–i and 7 (General Procedure). A solution of isothiocyanate (5 mM) in anhydrous toluene

(23) The cycloaddition again takes place through an exo transition state as deduced from the coupling constants observed for H_{10b} in both isomers **5h** and **5i** (J = 10.2 and 10.8 Hz, respectively).

(24) For related intramolecular cycloadditions of heterodienes involving preferentially an exo transition state, see: Reference 6a,b.

(25) For examples showing the influence of nonbonded interactions in the transition state, see for instance: Reference 4b and references cited therein.

(26) Barluenga, J.; Aguilar, E.; Olano, B.; Fustero, S. *J. Org. Chem.* **1988**, *53*, 1741.

(27) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(5 mL) was added dropwise to a solution of *N*-(trimethylsilyl)-imine (**2a–d** or **2f**) in anhydrous toluene (20 mL) at rt and the resulting mixture heated at 90 °C. After 10 h, the reaction mixture was cooled, shaken with water (50 mL), and extracted with dichloromethane; the organic layer was dried over sodium sulfate, filtered, and evaporated at reduced pressure. The cycloadducts thus obtained were purified by recrystallization from *n*-hexane–chloroform (5:1) (compounds **5b–c**) or subjected to flash chromatography (toluene/ether (10:1); compounds **5a**, **5d–i**, and **7**). Reaction yields and mp are given in Table II.

2-(Phenylimino)-1,2,3,4,4a,10b-hexahydro-5*H*-[1]benzopyrano[4,3-*d*][1,3]thiazine (5a): IR (Nujol) 3310, 1650 cm^{-1}; ^1H NMR δ 2.1 (m, 1 H), 2.7 (t, J = 11.5 Hz, 1 H), 2.95 (dd, J = 11.5, 5.2 Hz, 1 H), 3.75 (t, J = 11.1 Hz, 1 H), 4.2 (dd, J = 11.1, 1.7 Hz, 1 H), 4.25 (d, J = 10.3 Hz, 1 H), 5.6 (br s, NH), 6.8 (dd, J = 8.1, 1.1 Hz, 1 H, Ar), 7.0 (m, 2 H, Ar), 7.15 (m, 1 H, Ar), 7.25 (m, 2 H, Ar), 7.4 (d, J = 7.9 Hz, 2 H, Ar), and 7.6 (d, J = 7.38 Hz, 1 H, Ar); ^{13}C NMR δ 153.6 (s), 149.1 (s), 140.6 (s), 128.6 (d), 127.9 (d), 127.7 (d), 124.9 (s), 122.2 (d), 120.9 (d), 119.4 (d), 116.0 (d), 68.3 (t), 55.7 (d), 30.7 (d), and 28.1 (t); MS m/e 296 (M^+, 52), 263 (11), 204 (44), 131 (100), and 77 (89). Anal. Calcd for $C_{17}H_{16}N_2OS$: C, 68.89; H, 5.44; N, 9.45. Found: C, 69.12; H, 5.17; N, 9.48.

4-Phenyl-2-(phenylimino)-1,2,3,4,4a,10b-hexahydro-5*H*-[1]benzopyrano[4,3-*d*][1,3]thiazine (5b): IR (KBr) 3330, 1660 cm^{-1}; ^1H NMR δ 2.4 (m, 1 H), 3.8 (t, J = 11.0 Hz, 1 H), 4.1 (dd, J = 11.0, 3.5 Hz, 1 H), 4.3 (d, J = 11.2 Hz, 1 H), 4.6 (d, J = 10.2 Hz, 1 H), and 6.8–7.9 (m, 14 H, 13 Ar, 1 NH); ^{13}C NMR δ 153.8 (s), 149.3 (s), 140.5 (s), 138.7 (s), 129.0 (d), 128.8 (d), 128.5 (d), 128.2 (d), 128.1 (d), 127.8 (d), 124.8 (s), 122.5 (d), 121.0 (d), 119.4 (d), 116.1 (d), 67.0 (t), 57.1 (d), 48.9 (d), and 38.1 (d); MS m/e 372 (M^+, 19), 339 (100), 131 (50), and 77 (29). Anal. Calcd for $C_{23}H_{20}N_2OS$: C, 74.16; H, 5.41; N, 7.52. Found: C, 74.31; H, 5.20; N, 7.49.

2-[(4-Chlorophenyl)imino]-4-phenyl-1,2,3,4,4a,10b-hexahydro-5*H*-[1]benzopyrano[4,3-*d*][1,3]thiazine (5c): IR (KBr) 3330, 1640 cm^{-1}; ^1H NMR δ 2.3 (m, 1 H), 3.8 (t, J = 11.0 Hz, 1 H), 4.1 (dd, J = 11.0, 3.6 Hz, 1 H), 4.3 (d, J = 11.3 Hz, 1 H), 4.6 (d, J = 11.2 Hz, 1 H), and 6.8–7.8 (m, 14 H, 13 Ar, 1 NH); ^{13}C NMR δ 153.9 (s), 150.4 (s), 139.1 (s), 138.3 (s), 129.2 (d), 128.8 (d), 128.7 (d), 128.4 (d), 127.9 (d), 127.7 (s), 124.1 (s), 121.2 (d), 116.3 (d), 66.9 (t), 56.8 (d), 49.1 (d), and 38.4 (d); MS m/e 406 (M^+, 28), 373 (88), 280 (19), 131 (97), 91 (62), and 32 (100). Anal. Calcd for $C_{23}H_{19}ClN_2OS$: C, 67.89; H, 4.71; N, 6.88. Found: C, 68.05; H, 4.49; N, 6.83.

2-(Ethylimino)-4-phenyl-1,2,3,4,4a,10b-hexahydro-5*H*-[1]benzopyrano[4,3-*d*][1,3]thiazine (5d): IR (Nujol) 3330, 1660 cm^{-1}; ^1H NMR δ 1.25 (t, J = 7.2 Hz, 3 H), 2.4 (m, 1 H), 3.4 (m, 2 H), 3.8 (t, J = 11.0 Hz, 1 H), 4.05 (dd, J = 11.0, 3.6 Hz, 1 H), 4.3 (d, J = 11.3 Hz, 1 H), 4.55 (d, J = 10.1, 1 H), 6.8 (dd, J = 8.1, 1.2 Hz, 1 H, Ar), 7.0–7.9 (m, 8 H, 7 Ar, 1 NH), and 7.9 (d, J = 7.7 Hz, 1 H, Ar); ^{13}C NMR δ 153.6 (s), 152.5 (s), 139.3 (s), 128.9 (d), 128.1 (d), 127.8 (d), 127.7 (d), 125.3 (s), 120.8 (d), 115.7 (d), 67.0 (t), 56.4 (d), 48.2 (d), 38.2 (d), 37.0 (t), and 14.5 (q); MS m/e 324 (M^+, 20), 291 (71), and 131 (100). Anal. Calcd for $C_{19}H_{20}N_2OS$: C, 70.34; H, 6.21; N, 8.63. Found: C, 70.53; H, 6.09; N, 8.47.

4-Phenyl-2-(phenylimino)-1,2,3,4,4a,5,6,10b-octahydronaphtho[1,2-*d*][1,3]thiazine (5e): IR (Nujol) 3310, 1660 cm^{-1}; ^1H NMR δ 1.5 (m, 1 H), 1.8 (m, 1 H), 2.15 (m, 1 H), 2.8 (m, 2 H), 4.35 (d, J = 10.8 Hz, 1 H), 4.55 (d, J = 9.9 Hz, 1 H), 6.9–7.5 (m, 14 H, 13 Ar, 1 NH), and 7.9 (d, J = 7.4 Hz, 1 H, Ar); ^{13}C NMR δ 149.3 (s), 141.5 (s), 140.1 (s), 138.4 (s), 135.8 (s), 128.9 (d), 128.7 (d), 128.2 (d), 128.1 (d), 127.9 (d), 127.7 (d), 126.4 (d), 126.3 (d), 122.2 (d), 119.7 (d), 60.5 (d), 52.8 (d), 41.3 (d), 28.9 (t), and 26.0 (t); MS m/e 370 (M^+, 28), 337 (100), 115 (52), 91 (91), and 32 (58). Anal. Calcd for $C_{24}H_{22}N_2S$: C, 77.80; H, 5.98; N, 7.56. Found: C, 77.92; H, 6.25; N, 7.29.

2-(Ethylimino)-4-phenyl-1,2,3,4,4a,5,6,10b-octahydronaphtho[1,2-*d*][1,3]thiazine (5f): IR (Nujol) 3330, 1630 cm^{-1}; ^1H NMR δ 1.2 (t, J = 7.0 Hz, 3 H), 1.3 (m, 1 H), 1.65 (m, 1 H), 1.8 (m, 1 H), 2.7 (m, 2 H), 3.4 (m, 2 H), 4.25 (d, J = 10.8 Hz, 1 H), 4.35 (d, J = 9.9 Hz, 1 H), 6.9–7.4 (m, 9 H, 8 Ar, 1 NH), and 7.9 (d, J = 7.5 Hz, 1 H, Ar); ^{13}C NMR δ 152.5 (s), 140.3 (s), 138.9 (s), 135.6 (s), 128.7 (d), 128.2 (d), 128.0 (d), 127.9 (d), 127.8 (d), 126.3 (d), 126.1 (d), 60.2 (d), 52.2 (d), 41.2 (d), 37.2 (t), 28.8 (t), 26.1 (t), and 14.6 (q); MS m/e 322 (M^+, 42), 289 (100), 130 (75), 129 (80), 115 (74), 91 (92), and 32 (53). Anal. Calcd for $C_{20}H_{22}N_2S$: C, 74.49; H, 6.88; N, 8.69. Found: C, 74.32; H, 6.91; N, 9.02.

2-(Cylcohexylimino)-1,2,3,4,4a,10b-hexahydro-5*H*-[1]-benzopyrano[4,3-*d*][1,3]thiazine (5g): IR (Nujol) 3320, 1640 cm^{-1}; ^1H NMR δ 0.8–1.9 (m, 10 H), 2.0 (m, 1 H), 2.6 (t, J = 11.4 Hz, 1 H), 2.7 (dd, J = 11.4, 5.1, 1 H), 3.6 (t, J = 10.8, 2 H), 4.0 (d, J = 10.3 Hz, 1 H), 4.1 (dd, J = 10.8, 3.7 Hz, 1 H), 6.7 (d, J = 8.1 Hz, 1 H, Ar), 6.9–7.2 (m, 2 H, Ar, 1 NH), and 7.6 (d, J = 7.6 Hz, 1 H); ^{13}C NMR δ 153.4 (s), 149.1 (s), 127.1 (d), 126.7 (d), 125.5 (s), 119.7 (d), 114.9 (d), 68.0 (t), 55.3 (d), 50.4 (d), 32.9 (t), 32.7 (t), 30.6 (d), 27.6 (t), 25.5 (t), 24.7 (t), and 24.6 (t); MS m/e 302 (M^+, 36), 261 (34), 131 (60) and 41 (100). Anal. Calcd for $C_{17}H_{22}N_2OS$: C, 67.51; H, 7.33; N, 9.26. Found: C, 67.34; H, 7.69; N, 8.92.

4-Methyl-2-(phenylimino)-1,2,3,4,4a,10b-hexahydro-5*H*-[1]benzopyrano[4,3-*d*][1,3]thiazines (5h and 5i): IR (Nujol) 3320, 1640 cm^{-1}; NMR signals in the aliphatic region. **5h** (major stereoisomer): ^1H NMR δ 1.45 (d, J = 6.6 Hz, 3 H), 1.7 (m, 1 H), 3.4 (dq, J = 10.4, 6.6, 1 H), 3.85 (t, J = 11.1, 1 H), 4.4 (d, J = 10.2 Hz, 1 H), and 4.50 (dd, J = 11.1, 3.7, 1 H); ^{13}C NMR δ 66.9 (t), 57.1 (d), 39.0 (d), 38.7 (d), and 21.3 (q). **5i** (minor stereoisomer): ^1H NMR δ 1.4 (d, J = 6.9 Hz, 3 H), 2.3 (m, 1 H), 3.6 (qd, J = 6.9, 4.7, 1 H), 4.0 (t, J = 11.0 Hz, 1 H), 4.3 (dd, J = 11.0, 3.5 Hz, 1 H), and 4.65 (d, J = 10.8 Hz, 1 H); ^{13}C NMR δ 67.2 (t), 50.0 (d), 36.4 (d), 34.6 (d), and 18.2 (q); MS m/e 310 (M^+, 58), 277 (18), 218 (40), 131 (100), and 77 (98). Anal. Calcd for $C_{18}H_{18}N_2OS$: C, 69.65; H, 5.84; N, 9.02. Found: C, 69.41; H, 5.90; N, 8.89.

2-(Phenylimino)-1,2,3,4,4a,5,6,10b-octahydroindolizino-[8,7-*d*][1,3]thiazine (7): IR (Nujol) 3340, 1650 cm^{-1}; ^1H NMR δ 1.4–1.8 (m, 3 H), 2.75 (m, 2 H), 3.7 (td, J = 12.1, 4.3 Hz, 1 H), 3.8 (m, 1 H), 4.1 (d, J = 9.7 Hz, 1 H), 6.1 (m, 2 H), 6.4 (br s, 1 H), 6.9 (t, J = 7.0 Hz, 1 H), and 7.2 (m, 5 H); ^{13}C NMR δ 148.8 (s), 142.9 (s), 130.5 (s), 128.4 (d), 122.2 (d), 118.8 (d), 108.3 (d), 103.9 (d), 55.0 (d), 44.1 (t), 33.1 (d), 31.6 (t), and 28.2 (t); MS m/e 283 (M^+, 35), 191 (40), 118 (81), and 77 (100), and 51 (60). Anal. Calcd for $C_{16}H_{17}N_3S$: C, 67.81; H, 6.05; N, 14.83. Found: C, 67.79; H, 6.42; N, 14.65.

Preparation of Methylated Derivatives 6a and 6b. A solution of **5a** or **5b** (2 mM) in dry DMF (20 mL) was added dropwise to an ice-cooled suspension of NaH (0.05 g, 2.2 mM) in DMF (10 mL). The resulting mixture was stirred at rt for 1 h and then treated with MeI (0.19 mL, 3 mM) for 18 h at rt. Then, cold water (10 mL) was added, the mixture stirred, and extracted with dichloromethane. The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to give compounds **6a** and **6b** as yellow solids that were recrystallized from *n*-hexane–chloroform (5:1) (the reaction yields and mp are collected in Table II).

2-(*N*-Methyl-*N*-phenylamino)-3,4,4a,10b-tetrahydro-5*H*-[1]benzopyrano[4,3-d][1,3]thiazine (6a): IR (KBr) 1650 cm^{-1}; ^1H NMR δ 1.9 (m, 1 H), 2.7 (t, J = 11.6 Hz, 1 H), 2.8 (dd, J = 11.6, 4.8 Hz, 1 H), 3.3 (s, 3 H), 3.8 (t, J = 11.0 Hz, 1 H), 4.2 (dd, J = 10.8, 4.3, 1 H), 4.25 (d, J = 10.3 Hz, 1 H), 6.7 (dd, J = 8.0, 0.8 Hz, 1 H, Ar), 6.9 (td, J = 7.4, 0.8 Hz, 1 H, Ar), 7.1 (td, J = 7.4, 0.8 Hz, 1 H, Ar), 7.2–7.3 (m, 5 H, Ar), and 7.8 (d, J = 7.7 Hz, 1 H, Ar); ^{13}C NMR δ 153.7 (s), 151.9 (s), 144.7 (s), 129.0 (d), 128.5 (d), 127.9 (d), 127.8 (d), 127.0 (d), 126.1 (s), 120.8 (d), 115.9 (d), 69.0 (t), 56.0 (d), 39.5 (q), 30.4 (d), and 28.8 (t); MS m/e 310 (M^+, 32), 204 (40), 131 (100), and 77 (92). Anal. Calcd for $C_{18}H_{18}N_2OS$: C, 69.65; H, 5.84; N, 9.02. Found: C, 69.32; H, 5.81; N, 8.88.

2-(*N*-Methyl-*N*-phenylamino)-4-phenyl-3,4,4a,10b-tetrahydro-5*H*-[1]benzopyrano[4,3-*d*][1,3]thiazine (6b): IR (KBr) 1660 cm^{-1}; ^1H NMR δ 2.3 (m, 1 H), 3.4 (s, 3 H), 3.8 (t, J = 11.0 Hz, 1 H), 4.1 (dd, J = 11.0, 3.5 Hz, 1 H), 4.2 (d, J = 11.2 Hz, 1 H), 4.6 (d, J = 10.1 Hz, 1 H), 6.8 (d, J = 7.0 Hz, 1 H, Ar), 7.0–7.4 (m, 12 H, Ar), and 7.9 (d, J = 7.0 Hz, 1 H); ^{13}C NMR δ 153.8 (s), 152.5 (s), 144.3 (s), 138.3 (s), 128.9 (d), 128.8 (d), 128.5 (d), 128.3 (d), 128.0 (d), 127.9 (d), 127.8 (d), 127.0 (d), 126.0 (s), 120.7 (d), 115.8 (d), 67.4 (t), 57.2 (d), 48.9 (d), 39.5 (q), and 37.0 (d); MS m/e 386 (M^+, 28), 385 (37), 353 (90), 280 (23), 132 (67), 131 (100), 91 (55), and 77 (73). Anal. Calcd for $C_{24}H_{22}N_2OS$: C, 74.58; H, 5.74; N, 7.25. Found: C, 74.68; H, 5.66; N, 7.40.

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Registry No. **1a**, 28752-82-1; (*E*)-**1d**, 28809-05-4; (*Z*)-**1d**, 28809-09-8; **1e**, 38002-87-8; **1f**, 135192-15-3; **2a**, 126797-54-4; **2b**, 135192-03-9; **2c**, 135192-04-0; (*E*)-**2d**, 135192-05-1; (*Z*)-**2d**, 135192-14-2; **2e**, 135192-06-2; **2f**, 126797-60-2; **5a**, 126797-57-7; **5b**, 135192-07-3; **5c**, 135192-08-4; **5d**, 135192-09-5; **5e**, 135192-10-8; **5f**, 135192-11-9; **5g**, 126797-58-8; **5h**, 135192-12-0; **5i**, 135269-28-2; **6a**, 126797-59-9; **6b**, 135192-13-1; **7**, 126797-62-4; phenyl isothiocyanate, 103-72-0; 4-chlorophenyl isothiocyanate, 2131-55-7; ethyl isothiocyanate, 542-85-8; cyclohexyl isothiocyanate, 1122-82-3.

Mesoions as Versatile Intermediates in Tetrathiafulvalene Synthesis

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Fourteen new alkylthio-substituted tetrathiafulvalene (TTF) donors have been prepared via the mesoionic 2-(*N*,*N*-dialkylamino)-5-methyl-1,3-dithiolium-4-thiolates **4**. By S-alkylation with alkyl halogenides and alkyl dihalogenides, **4** was transformed into a variety of mono- and bis-1,3-dithiolium salts **5**. Coupling of **5** with the anion of 4,5-dimethyl-2*H*-1,3-dithiole-2-phosphonate ester **6** yielded a series of bis(tetrathiafulvalenes) **2** and (alkylthio)tetrathiafulvalenes **3**. By conventional methods, **5** was coupled to bis(alkylthio)tetrathiafulvalenes. The synthesis of **4** was improved. An *N*,*N*-dialkyldithiocarbamate salt was allowed to react with a 2-halo carboxylic acid to yield a 1-(carboxyalkyl)-*N*,*N*-dialkyldithiocarbamate ester **10**, which was then transformed into **4**. The electrochemistry of the new TTFs is reported.

Introduction

Tetrathiafulvalenes (TTFs) **1** are widely employed as π-electron donors for the formation of highly conducting charge-transfer salts or binary cation radical salts.[1] The physical properties of these solids depend strongly on the electronic and structural properties of the TTF unit, i.e., on the substituent pattern.

We report the preparation of two series of asymmetrically substituted TTFs, so-called dimeric TTFs **2**, and TTFs carrying long alkylthio or (carboxyalkyl)thio substituents **3**.

In most cases such a series of asymmetrically substituted TTFs has been obtained by statistical cross-coupling of two different 1,3-dithioles. The desired compounds were then isolated from the mixture of TTFs by tedious fractional recrystallization and/or chromatographic methods.[2-4]

Our synthetic strategy was to prepare the desired compounds via the mesoions **4**, which can now be obtained easily (see below). The mesoions are then S-alkylated to form 2-amino-5-(alkylthio)-1,3-dithiolium salts **5**. Compounds **5** serve as substrates in a selective Horner–Emmons-type coupling[5] to yield asymmetrically substituted TTFs **2** and **3**.

Scheme I

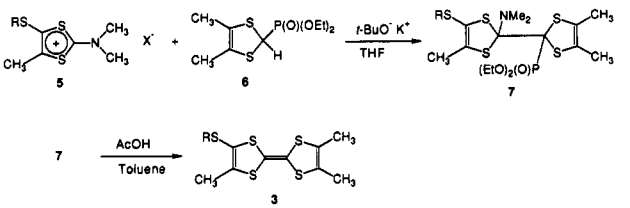
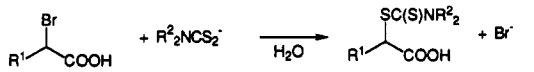


Table I. 1-(Carboxyalkyl)-*N*,*N*-dialkyldithiocarbamate Esters 10a–e



compd no.	R^1	R^2
10a	CH_3	CH_3
10b	$(CH_2)_3CH_3$	CH_3
10c	$(CH_2)_{15}CH_3$	CH_3
10d	Ph	CH_3
10e	CH_3	$-(CH_2)_5-$

We have targeted the dimeric TTFs **2**[6] since the $-S-(CH_2)_nS-$ link presumably gives rise to only a negligible electronic interaction between the two TTF subunits of the total molecule in the solid state, which may lead to interesting electronic properties of the solids due to the spatial degeneracy of the π-system.[6a,7] The interaction may also have interesting electrochemical consequences in solution (see below).

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