Addition of Twisted 1,1-Bis(thioacyl)-2,2-diaminoethylenes to Dimethyl Acetylenedicarboxylate. 2. Structure Determination of Two Isomeric Spiro Adducts by X-ray Crystallography and of a Rearrangement Product by the 2D INADEQUATE Technique†

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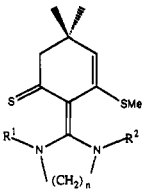
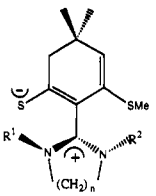
1,3-Dialkyl-2-(4,4-dimethyl-2,6-dithioxocyclohexylidene)imidazolidines (twisted push–pull ethylenes) react smoothly with dimethyl acetylenedicarboxylate (DMAD) but require at least 3 equiv of DMAD for complete consumption. Chromatography of the complex reaction mixture gave two isomeric 1:2 adducts, shown by X-ray crystallography to be (*E*)- and (*Z*)-[1,2-bis(methoxycarbonyl)vinyl]thio-susbstituted thiopyran-4-spiro-2′-imidazolidines. Treatment of the spiro compounds with dilute nonaqueous acid led to isomers in which the imidazolidine ring had opened, and acid hydrolysis gave a thiopyrone and its enol tautomer. Continued chromatography of the original reaction mixture gave three new compounds, a thiopyran-4-thione, a tetrakis(methoxycarbonyl)-1,4-dithiaphenalene, and a precursor to this with the same ring system. The formation of these compounds requires migration of a sulfur atom from the cyclohexene ring to the annelated thiopyran ring, and a possible mechanism is discussed. The dithiaphenalene structure was firmly established by the 2D INADEQUATE technique.

In previous works,[3] we have studied push–pull ethylenes with thiocarbonyl groups as electron attractors, and we have recently[4] described the synthesis of a series of 1,3-dialkyl-2-[2-(methylthio)-4,4-dimethyl-6-thioxocyclohex-2-enylidene]imidazolidines and -hexahydropyrimidines **1**.



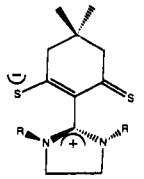
1a



1b

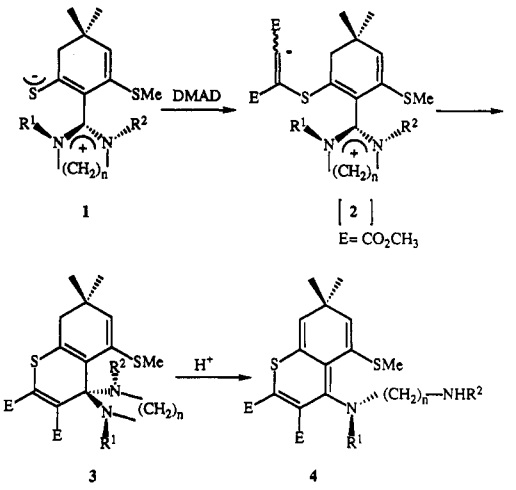
Compounds **1** are twisted about the double bond, and the barrier to passage through the planar state was found to be >28 kcal/mol. These compounds are therefore better described by the betainic structure **1b** than by **1a**. They are neutral dipolar compounds and strong nucleophiles, and their reactions in nucleophilic additions were considered of interest. Their reaction with dimethyl acetylenedicarboxylate (DMAD) probably proceeds in steps with nucleophilic addition of C–S⁻ to form a vinyl anion **2** as the first step, followed by addition of this anion to the amidinium carbon atom in [N–C–N]⁺ to give a spiro compound **3** as indicated in Scheme I. Under weakly acidic conditions the spiro compounds undergo ring opening to give isomeric 4-aminothiopyran derivatives **4**.

The thioxocyclohexenylidene derivatives **1** were formed by S-methylation and facile deprotonation of the 2,6-dithioxo compounds **5** and the analogous hexahydropyrimidine derivatives. Compounds **5** are also betaines,



5 a, R = CH_2Ph
b, R = CH_3

Scheme I



1 **[2]** E = CO_2CH_3 **3** **4**

and a twist angle at the formal double bond of 80.8° was found in an X-ray crystallographic study of **5a**.[5] The negative charge is delocalized over the S–C–C–C–S moiety, and compounds **5** are good nucleophiles, although weaker than **1**, in which the negative charge is mainly localized on one sulfur atom. In this work, we discuss some of the nucleophilic addition reactions of compounds **5** to DMAD.

Results and Discussion

While compounds **1** reacted smoothly with 1 molar equiv of DMAD to give nearly quantitative yields of the spiro adducts **3**, reaction of **5a** with 1 molar equiv of DMAD (dropwise addition of a dilute solution of DMAD to a dilute

† Part 1: see ref 14.

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(3) (a) Khan, Agha Z.; Isaksson, R.; Sandström, J. *J. Chem. Soc., Perkin Trans. 2* **1987**, 491–495. (b) Khan, Agha Z.; Sandström, J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2085–2089.
(4) Khan, Agha Z.; Sandström, J. *J. Org. Chem.* **1991**, *56*, 1902–1907.
(5) Sandström, J.; Stenvall, K.; Sen, N.; Venkatesan, K. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1934–1942.

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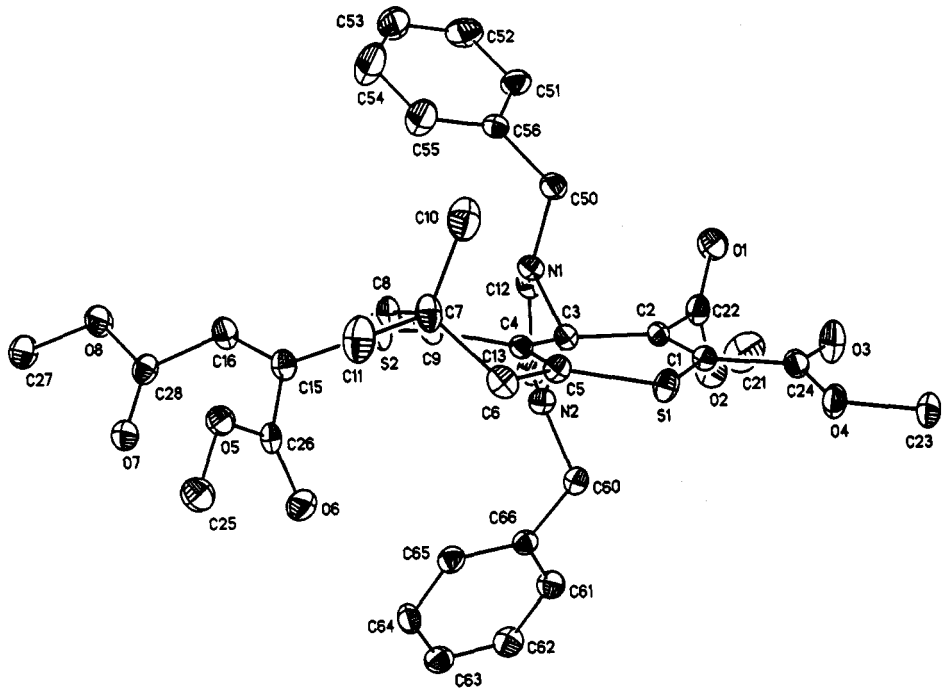


Figure 1. Picture of 8a*E* with atom numbers.

Table I. ^{1}H NMR Chemical Shifts for the Spiro Compounds 8 in $CDCl_3$ (Singlets Unless Otherwise Noted)

	8a*E*	8a*Z*	8b*E*	8b*Z*
H-3	5.99	5.67	5.83	5.60
H-5	2.27	2.18	2.25	2.15
H-7	1.12	1.02	1.04	0.98
H-9, H-10	2.82–3.02[a]	2.77–3.13[a]	2.91–3.26[a]	2.95–3.30[a]
H-14	6.08	6.46	5.96	6.26
N-CH_2Ph	3.77, 4.00 (12.9)[b]	3.85, 4.05 (12.9)[b]		
N-CH_3			2.34	2.39
CO_2CH_3	3.70, 3.74	3.72, 3.83	3.67, 3.78	3.70, 3.74
	3.79, 3.80	3.87, 3.89	3.79, 3.80	3.79, 3.80

[a] AA'BB' system. [b] J_{AB}/Hz.

solution of **5a**, solvent dry toluene or dry acetonitrile) gave a complex reaction mixture containing a large quantity of unreacted **5a**. In order to achieve complete consumption of **5a** it was necessary to add a total of at least 3 molar equiv of DMAD. From the reaction mixture a number of compounds could be isolated by column chromatography, which permit some conclusions about the reaction pathways.

The main products (up to 50% combined yields) were two isomers with the molecular formula $C_{37}H_{40}N_2O_8S_2$, which indicates that the compounds are 1:2 adducts of **5a** and DMAD. The isomers, (8a*E* and 8a*Z*), were obtained in nearly equal amounts, and they could be separated by repeated column chromatography and obtained in crystalline form. NMR spectra (Table I) indicate that they are analogues of the spiro compounds **3** with a [1,2-bis(methoxycarbonyl)vinyl]thio substituent in position 6, and the difference between them seemed to be in the geometry of the vinyl group. The ^{1}H chemical shifts of the vinylic proton (δ 6.08 and 6.46) allowed assignment of the isomers to the *E* and *Z* configurations on the basis of standard substituent effects.[6]

The proposed structures of the **8a** isomers were confirmed by single-crystal X-ray diffraction. The two compounds have very similar structures except for the vinylthio side chains. The thiopyran rings are very nearly planar, whereas the 1,3-cyclohexadiene rings are puckered. The NMR spectra indicate a plane of symmetry through the cyclohexadiene and thiopyran rings, but this must be due to fast inversion of the cyclohexadiene ring at ambient temperature in solution. The imidazolidine rings adopt flattened envelope conformations with the flap tip at the spiro carbon atom. The nitrogen atoms are pyramidalized with the base of the pyramid toward the ester group at C-11 in the thiopyran ring (C-2 in Figure 1). Pyramidalization angles between 31 and 39° were calculated[7] between the exocyclic N–C bonds and the adjacent C–N–C planes in the rings. The ester group at C-12 (C-1 in Figure 1) is coplanar with the thiopyran ring whereas that at C-11 is perpendicular due to the steric effect of the proximate imidazolidine ring.

Analogous spiro compounds were formed when **5b** reacted with DMAD, but only one of the stereoisomers, the *Z* form, could be isolated in pure form.

The first step in the reaction of compounds **5** with DMAD is in all likelihood the nucleophilic addition of S^- to DMAD to form a betaine with a vinyl carbanion group (**6**, Scheme II). Two alternative routes, A and B, can be envisaged for the next step.

In route A, the vinyl carbanion abstracts an allylic proton from the cyclohexene ring and forms two stereoisomers (7*E* and 7*Z*). The carbanionic carbon in **6** is

6*Z* 6*E*

probably sp^2 hybridized with *E* or *Z* configurations at the double bond and the negative charge in a lone pair orbital, and with fast exchange between the *E* and *Z* forms.[8] It

(6) Pretsch, E.; Clerc, T., Seibl, J.; Simon, W. *Spectral Data for Structure Determination of Organic Compounds*; Springer-Verlag: Berlin, 1983; p H220.

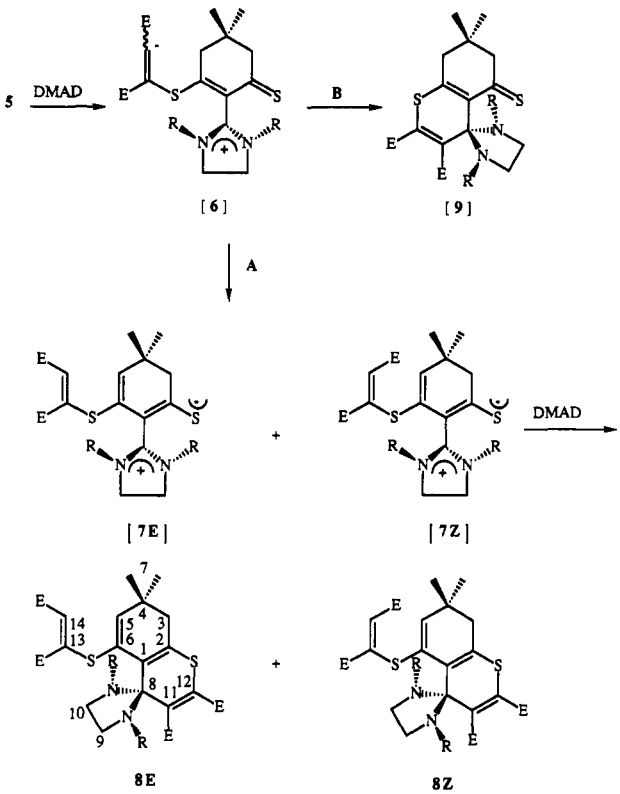
(7) (a) The pyramidalization angles were calculated according to Volland et al.,[7b] using the mean value of the very similar exocyclic C–N–C angles for χ. (b) Volland, W. W.; Davidson, E. R.; Borden, W. T. *J. Am. Chem. Soc.* **1979**, *101*, 533–537.

Table II. ^{1}H Chemical Shifts for Compounds 10 and 12 in $CDCl_3$ (Singlets Unless Otherwise Noted)

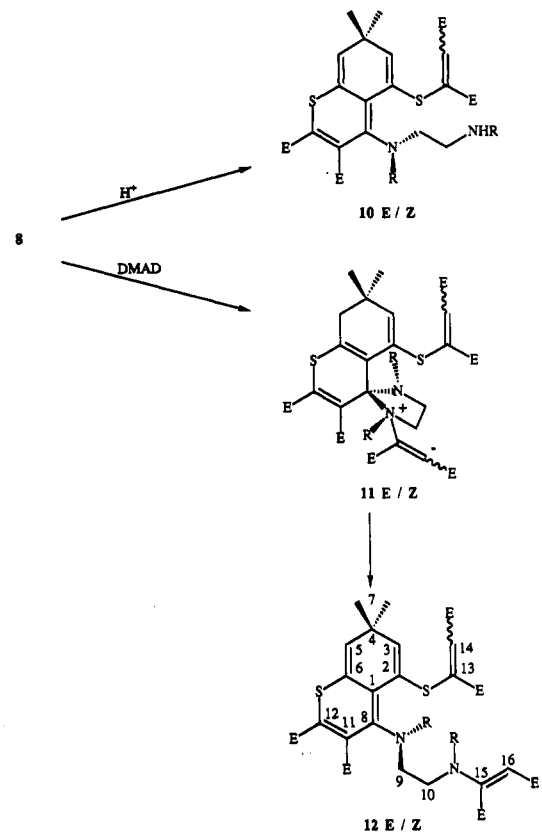
	10a*E*	10a*Z*	10b*E*	10b*Z*	12b*Z*
H-3, H-5	5.66, 6.34 (1.7)[a]	5.39, 5.88 (1.7)[a]	5.48, 6.34 (1.7)[a]	5.45, 6.09 (1.6)[a]	5.45, 5.92 (1.7)[a]
H-7	1.08, 1.11	0.93, 0.96	1.14, 1.17	1.11, 1.16	1.08[b]
H-9, H-10	2.70 (t), 2.92 (m)	2.81 (t), 3.09 (m)	2.77–3.13 (m)	3.01–3.37 (m)	2.96 (t), 3.36 (m)
H-14	5.95	6.36	5.89	6.45	6.45
H-16					4.59
N-CH_2Ph	3.70	3.71			
	4.13, 4.26 (13.6)[a]	4.11, 4.19 (13.0)[a]			
N-CH_3			2.57, 2.69	2.66, 2.74	2.62, 2.82
CO_2CH_3	3.64, 3.68	3.61, 3.68	3.64, 3.68	3.79, 3.80	3.60, 3.75
	3.68, 3.78	3.78, 3.79	3.68, 3.78	3.82, 3.83	3.78, 3.79
					3.82, 3.90

[a] J_{AB}/Hz. [b] Accidental overlap.

Scheme II



Scheme III



seems natural that the *E* form makes an intramolecular and the *Z* form an intermolecular proton abstraction. Compounds **7** are analogues of **1** and should be stronger nucleophiles than **5**, as discussed in the previous text. In the next step, compounds **7** add rapidly to a second molecule of DMAD, also in this case with vinyl anions as likely intermediates, which cyclize to the spiro compounds **8***E* and **8***Z*.

In ethanol or acetonitrile solution containing HCl the spiro compounds **8***E* are rearranged to the isomeric compounds **10***E* and similarly **8***Z* to **10***Z*. The spectroscopic data (Table II) show that compounds **10** are analogues of **4**, i.e., are formed by opening of the imidazolidine ring by breaking of a C(spiro)–N bond and transfer of a proton from the cyclohexadiene CH_2 group to the nitrogen atom (Scheme III).

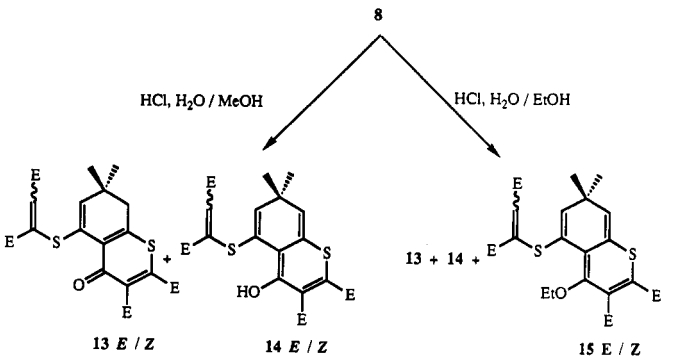
As was the case with compounds **4**, the 8-amino group (numbering according to Scheme III) is rotated out of the plane of the thiopyran ring, leading to nonequivalence of diastereotopic nuclei in ^{1}H and ^{13}C NMR spectra. Bandshape analysis of the 7-methyl and benzylic proton resonances of **10a***E* and **10a***Z* in the temperature range 50–85 °C gave free energy barriers of 17.6 kcal/mol for both compounds, quite similar to the value found for **4** (17.8 kcal/mol).[4]

In the chromatographic workup, small amounts of compounds were found (**12***E*/*Z*, Scheme III), which could have been formed by reaction of **5** with 3 equivs of DMAD. Analogous compounds were described in ref 4. Since no free DMAD is present in the final reaction mixture before the chromatography, it seems that either compounds **8** undergo slow ring opening to **10** and then add to DMAD to give **12** during the reaction or that formation of **12** is initiated by attack of a nitrogen lone pair on a DMAD molecule to form a betain (**11**, Scheme III), which then opens the imidazolidine ring and undergoes proton transfer to give **12**. Winterfeldt[9] has shown that addition of tertiary amines to methyl propiolate gives ammonium adducts, which may be stabilized by cleavage of C–N bonds.

(8) (a) Caramella, P.; Houk, K. N. *Tetrahedron Lett.* **1981**, *22*, 819–822. (b) Walborsky, H. M.; Turner, L. M. *J. Am. Chem. Soc.* **1972**, *94*, 2273–2279. (c) Jung, M. E.; Buszek, K. R. *J. Am. Chem. Soc.* **1988**, *110*, 3965–3969.

(9) Winterfeldt, E. *Chem. Ber.* **1964**, *97*, 1952–1958.

Scheme IV

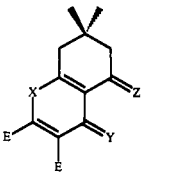


Treatment of the spiro compounds 8*E* and 8*Z* with aqueous methanolic HCl led to hydrolysis of the imidazolidine ring (an aminal structure) and formation of the stereoisomeric thiopyrones 13*E* and 13*Z* (Scheme IV). The same compounds were obtained by hydrolysis of compounds **10**. When the reaction was performed in ethanolic HCl, the enol ether **15** was also formed. Isomers of 13*E* and 13*Z* were also isolated and identified as the vinylogous enols 14*E* and 14*Z*. Corresponding compounds were not found on hydrolysis of **3**, which may be due to the higher reaction temperature employed, which leads to the thermodynamically more stable keto tautomers.

Continued chromatography of the reaction mixtures from compounds **5** and DMAD gave four compounds, which are given the symbols I, II, III, and IV. The first of these, I, is a dark green, crystalline compound $C_{15}H_{16}O_5S_2$, which was formed in up to 30% yield when **5b** reacted with DMAD in toluene (but not in acetonitrile). According to ^1H and ^{13}C NMR spectra, it contains a dimethylcyclohexenone or -thione residue and a DMAD residue and it should be formed by reaction of one molecule of **5b** with one molecule of DMAD and one molecule of water accompanied by elimination of one molecule of *N,N'*-dimethylethylenediamine. Since water is absent in the reaction mixture, I must be formed in the chromatographic workup from **9** (Scheme II) or from another unobserved precursor by reaction with water bound in the silica.

The first structure to be considered for I is the thiopyran-4-one **16**, which could be formed simply by hydrolysis of **9**. However, the IR and NMR spectral data for I are not in agreement with structure **16**. The IR spectra of the similar thiopyrone **17**[4] and pyrone **18**[10] show two and one strong bands, respectively, in the range 1720–1740 cm^{-1}, assigned to the ester carbonyl stretching vibrations, and one band at ca. 1700 cm^{-1}, assigned to the cyclohexenone carbonyl group. Thiopyrone and pyrone carbonyl bands appear at 1610 and 1645 cm^{-1}, respectively, for **17** and **18**. The spectrum of I shows ester carbonyl bands at 1732 and 1722 cm^{-1}, a third carbonyl band at 1698 cm^{-1}, and then no bands at lower frequency until 1550 cm^{-1}. This points to the absence of a thiopyrone carbonyl group and to the presence of a carbonyl group in the cyclohexene ring.

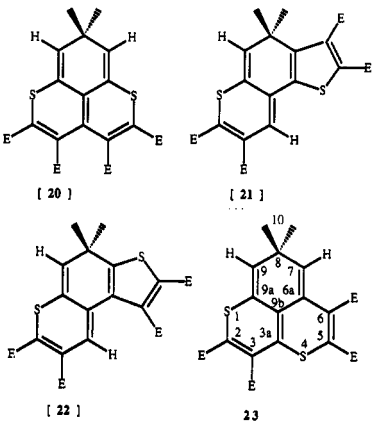
The ^{13}C NMR spectra give further information, in particular the carbonyl resonances. Each of I, **17**, and **18** displays two ester carbonyl resonances in the range δ 159.0–165.0. Thiopyrone and pyrone carbonyl resonances for **17** and **18** appear at δ 174.8 and 176.0, and the corresponding cyclohexenone carbonyl resonances at δ 191.1 and 192.2, respectively. Compound I, however, has CO/CS



16 X = Z = S, Y = O
17 X = S, Y = Z = O
18 X = Y = Z = O
19 X = Y = S, Z = O

resonances at δ 192.4 and 198.4, none of them in the range expected for a thiopyrone carbonyl. The ^1H–^{13}C correlations were determined by HETCOR and COLOC experiments (see Experimental Section), and the resonance at 192.3 ppm was found to originate from a carbon atom attached to a CH_2 group. Evidently, both IR and ^{13}C NMR data indicate a 2,3-bis(methoxycarbonyl)-5-acylthiopyran-4-thione structure **19**. This structure requires migration of a sulfur atom from the cyclohexene ring to the thiopyran ring. We have at present no mechanism to propose for this reaction.

The second compound, II, was obtained as dark brown crystals in yields of up to 30% from **5a** and **5b** both with toluene and with acetonitrile as solvent. The molecular formula was found to be $C_{21}H_{20}O_8S_2$, and according to the ^1H and ^{13}C NMR spectra it contains four nonequivalent ester groups and two vinylic protons forming an AX system. It is formally obtained from one molecule of **5a** and two molecules of DMAD with elimination of one molecule of *N,N'*-dialkylethylenediamine. The closest structure for this compound should be **20**, but evidently the C_{2v} sym-



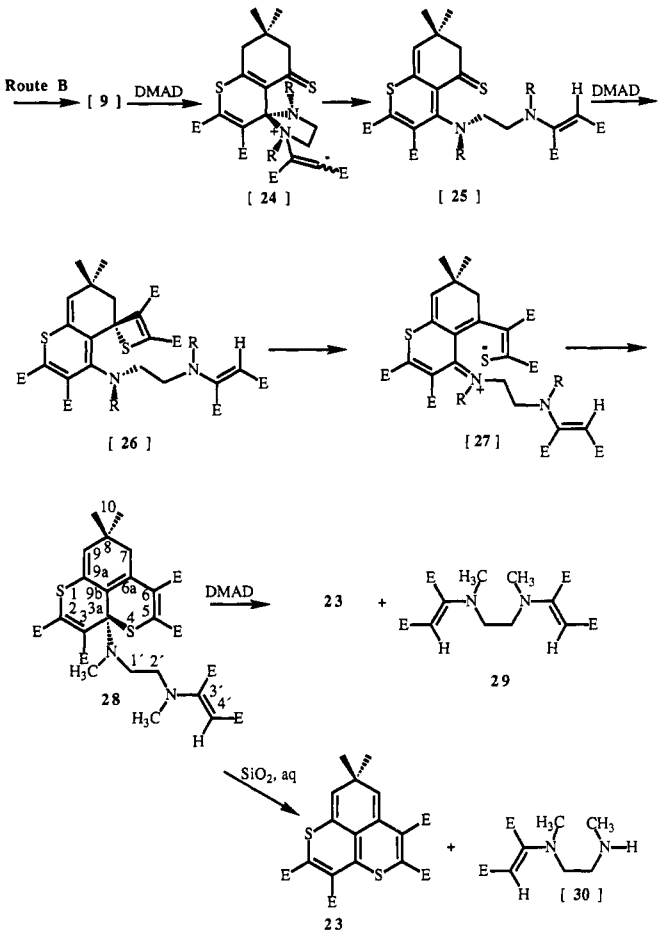
metry of this structure does not conform with the observed ^1H and ^{13}C NMR spectra, which correspond to C_s symmetry, as evidenced by the equivalence of the two *C*-methyl groups but nonequivalence of all other groups. We have considered three alternative structures with C_s symmetry, **21**, **22**, and **23**. Structure **21** could arise through addition of C=S in **9** to DMAD, followed by a Michael addition, proton migrations, and elimination of the diamine with or without intervention of DMAD. Structure **22** contains the same structural elements as **21**, but no route for its formation is proposed. Structure **23** requires migration of a sulfur atom from the cyclohexene to the thiopyran ring.

The connectivities between all carbon atoms except the ester methoxy groups could be established by a series of 2D INADEQUATE experiments.[11] These experiments confirmed structure **23**, and a possible reaction route

(10) Khan, Agha Z.; Bergquist, K.-E.; Sandström, J. *Acta Chem. Scand.* **1990**, *44*, 833–836.

(11) (a) Bax, A.; Freeman, R.; Kempsell, S. P. *J. Am. Chem. Soc.* **1980**, *102*, 4849–4851. (b) Bax, A. *Two-dimensional Nuclear Magnetic Resonance in Liquids*; Delft University Press: Reidel Publishing: Dordrecht, 1984; p 157–165.

Scheme V



leading to this structure will be discussed later (Scheme V).

The third compound, III, was obtained in low and varying yields from reactions in toluene with **5b** as starting material, as a brownish labile solid, which on each chromatographic purification was partly transformed to compound **23**. The molecular formula of III is $C_{31}H_{38}N_2O_{12}S_2$, indicating that it is formed from one molecule of **5b** and three molecules of DMAD. The NMR spectra show six nonequivalent ester groups and two vinylic protons. One of these belongs to a strongly shielded CH group (δ_H 4.54, δ_c 84.08), which points at the presence of an aminomaleic ester residue. III has no symmetry elements, as indicated by the nonequivalence of the *C*-methyl groups ($\Delta\delta_H$ 0.14) and of the cyclohexadiene methylene protons ($\Delta\delta_{AB}$ 0.19, J_{AB} = 14.2 Hz) and by the observation that it is resolved into enantiomers by chromatography on swollen microcrystalline triacetylcellulose.[12] These results and the ready decomposition of III to give **23** are in agreement with structure **28**.

Compound IV, $C_{16}H_{24}N_2O_4$, crystallized spontaneously as colourless prisms in 6% yield from one of the chromatographic fractions. It was identified with compound **29** (Scheme V), already synthesized and studied by us.[10]

The formation of compounds II–IV may be explained by a sequence of reactions (Scheme V) starting along path B in Scheme II. The hypothetical spiro compound **9** is a weak S-nucleophile but may react with DMAD as a N-nucleophile to give the betaine **24**. Cleavage of one of the C–N bonds[9] gives the thione **25**, which is a stronger S-nucleophile than **9**. Addition of a second molecule of DMAD to **25** may give the thiete **26**, which rearranges to **28** with the betaine **27** as intermediate.[13] Addition of DMAD to **28** may lead to **23** and **29**. Besides, **23** is probably formed from **28** together with the unobserved aminomaleic ester **30** on chromatographic workup. Compound **19** cannot have been formed with **23** or **28** as intermediate, since treatment of **28** with silica gives only **23**, which is quite stable under these conditions. Compounds **23** is a representative of the unusual 1,4-dithiaphenalene ring system.

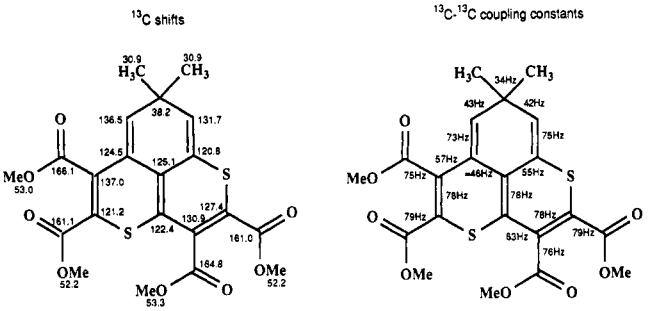


Figure 2. ^{13}C chemical shifts and ^{13}C–^{13}C couplings for **23** as determined by 2D INADEQUATE experiments.

As is discussed in the previous paper of this series,[14] it is essential that dry solvents are used, since traces of water lead to completely different products.

INADEQUATE Experiments. The structure of **23** was established and the alternative structures **20–22** were rejected on the basis of the ^{13}C–^{13}C connectivities detected in three different 2D INADEQUATE experiments.[11,15] One 2D experiment, which covered the range δ 117–169, outlines the carbon skeleton from the carbonyl carbons to the protonated olefinic carbons (C-7 and C-9) except for the connection between C-6a and C-9b. A second experiment, covering the saturated and olefinic carbon spectral region, established the connection between C-7 and C-8, between C-8 and C-9, and also between C-8 and the methyl carbons (C-10) at δ 30.9. C-6a and C-9b, at δ 124.5 and 125.1, respectively, constitute an AB spin system with $\Delta\sigma/J_{cc} \approx 1$, which gave low sensitivity in the two INADEQUATE experiments performed with $\tau = {}^1/_4J_{cc}$. In a third experiment performed with $\tau = {}^3/_4J_{cc}$, the inner lines of the AB system became clearly observable and proved the connection between C-6a and C-9b. The outer lines were too weak to allow a precise measurement of the coupling constant.

The connectivities and the corresponding coupling constants (Figure 2) prove the existence of a 1,4-cyclohexadiene ring with two methyl groups in position 3, hydrogen atoms in positions 2 and 4, one MeOCOC=CCO_2Me group attached to position 5, and one MeOCOC=$C(CO_2Me)C$= group attached to position 6. These data in combination with the molecular formula leave structure **23** as the only possibility and definitively exclude structures **20–22**. The ^{13}C chemical shifts and the ^{13}C–^{13}C coupling constants are consistent with the substitution pattern of **23**.

Experimental Section

^1H NMR spectra were recorded at 300 MHz and ^{13}C NMR spectra at 75 MHz. Signal assignments were performed with the

(12) Mannschreck, A.; Koller, H.; Wernicke, R. *Merck Kontakte* **1985**, *1*, 40–48.

(13) We are grateful to one of the reviewers for suggesting this mechanism.

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DEPT,[16] HETCOR,[15,17,18] and COLOC[19] pulse sequences and with the aid of standard substituent increments.[6] The 2D INADEQUATE experiments were performed as suggested by Bax[15] on a solution of **23** (0.40 g) in $CDCl_3$ (0.40 mL) at 35 °C for solubility reasons. The experiments were performed with the incremental delay between the conversion and read pulses and in a 128-step phase cycle. In the three experiments, the delay time for transfer into double-quantum coherence, τ, was calculated from $\tau = {}^1/_4J_{cc}$ with J_{cc} = 70 Hz and 45 Hz and from $\tau = {}^3/_4J_{cc}$ with J_{cc} = 60 Hz. More detailed information is given as supplementary material.

The chromatographic enantiomer resolution of **28** was performed with the equipment described by Isaksson and Roschester.[20]

X-ray Crystallography. The unit cell in the crystal of **8aE** was found to belong to the triclinic space group $P\bar{1}$ and to contain two molecules. The unit cell in the crystal of **8aZ** belongs to the monoclinic space group $P2_1/c$ and contains four molecules. The final refinement indices were R = 0.0471 and R_w = 0.0537 for **8aE** and R = 0.0664 and R_w = 0.0691 for **8aZ**.

Preparations. Of the starting materials **5a** and **5b**, the former has already been described.[5] **1,3-Dimethyl-2-(4,4-dimethyl-2,6-dithioxocyclohexylidene)imidazolidine (5b)** was obtained by addition of 2,4-bis[4-(methylthio)phenyl]-1,3,2,4-dithiadiphosphetane 2,4-disulfide[4] (4.37 g) to a solution of the 2,6-dioxo analogue of **5b**[21] (2.36 g) in 1,2-dimethoxyethane (50 mL) at ambient temperature. Spontaneous crystallization occurred within a few hours to give 2.42 g of orange prisms. Flash chromatography[22] of the mother liquor on silica (Merck 60) gave another crop of 0.13 g, total yield 95%, mp 248–250 °C after recrystallization from toluene–petroleum ether: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (s, 6 H, $(CH_3)_2C$), 2.70 (s, 4 H, $CH_2C{=}S$), 2.89 (s, 6 H, NCH_3), 3.83 (s, 4 H, CH_2N); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.61 ($(CH_3)_2C$), 33.48 (CH_2N), 33.72 ($(CH_3)_2C$), 49.24 (CH_3N), 57.47 ($CH_2C{=}S$), 129.00 ($C(C{=}S)_2$), 171.04 (CN_2), 205.71 (C=S); MS (70 eV, *m/e*) 268 (M^+, 62), 235 (100), 58 (55), 56 (80), 42 (81); high-resolution MS (M^+) found 268.1071, calcd for $C_{13}H_{20}N_2S_2$ 268.1068; UV (EtOH) 492 (300), 414 (20 500), 247s (4800), 230 (9900).

The addition of **5a** or **5b** to DMAD was typically performed as follows: A solution of DMAD (2.84 g) in dry toluene (200 mL) was added dropwise at a rate of ca. 1 mL/min with rapid stirring at ambient temperature under argon to a solution of **5a** (1.68 g) in dry toluene (200 mL). TLC showed that DMAD was consumed almost immediately, but all **5a** was not consumed until ca. 130 mL of the DMAD solution had been added. Workup started immediately. At this stage no significant excess of DMAD was present. The reaction mixture was concentrated under vacuum and subjected to flash chromatography on silica, using as the mobile phase first toluene, then toluene with gradually increasing concentration of ethyl acetate, then pure ethyl acetate, and finally ethyl acetate with gradually increasing concentration of methanol. TLC of the reaction mixture showed 10–15 colored spots, and continued column chromatography seemed to increase the number of products. The flash chromatography had to be repeated several times to obtain pure products, and the yields given are often lower than the real ones. The first product eluted was **8aE** (0.036 g), followed by a mixture of **8aE** and **8aZ** (0.97 g), which was rechromatographed to give pure **8aE** (0.51 g, total yield 19%) and **8aZ** (0.34 g, 12% yield). Continued chromatography gave **23** (0.46 g, 25% yield) followed by several colored compounds, which have not yet been identified.

When the experiment was repeated with dry acetonitrile as solvent, the same products were obtained in similar yields. When DMAD reacted with **5b** (2.68 g) in dry toluene as in the first experiment with **5a**, a 15:85 mixture of the triadducts **12bE** and **12bZ** (0.69 g, 10% yield) was first eluted, followed by a mixture of the spiro compounds **8bE** and **8bZ** (1.44 g, 26% yield). Continued chromatography gave successively **23** (0.88 g, 19% yield), **28** (0.35 g, 5% yield), **19** (0.61 g, 18% yield), **29** (0.14 g, 4% yield), and a mixture of **10bE** and **10bZ** (0.44 g, 8% yield).

In repeated experiments, the yields showed some variations due to difficulties to reproduce exactly the reaction conditions and the chromatographic separation procedure. **2,3-Bis(methoxycarbonyl)-5(*E*)-[[1,2-bis(methoxycarbonyl)vinyl]thio]-7,7-dimethyl-7,8-dihydro-1′,3′-dibenzylbenzo[*b*]thiopyran-4-spiro-2′-imidazolidine (8a*E*)** was obtained as pale yellow prisms, mp 186–188 °C after recrystallization from toluene. For NMR spectra, see Table I: MS (CI-NH_3) 705 (M^+ + 1, 82), 241 (68), 164 (100), 151 (40), 106 (100), 61 (56); elemental analysis C, H, N, S; UV (MeCN) 338 (9000), 282 (9250), 239 (13 000), 203 (42 000). The isomer **8aZ** was also obtained as pale yellow prisms, mp 107–108 °C after recrystallization from toluene: MS (CI-NH_3) 705 (M^+ + 1, 54), 255 (25), 241 (70), 164 (100), 147 (24), 106 (48). UV (MeCN) 323 (12 000), 292 (12 000), 237 (15 000), 200 (43 500). The *N*-methyl analogues **8bE** and **8bZ** showed very similar retention on chromatography, and the *E* form could not be obtained completely pure. It has been possible to identify all NMR resonances for both isomers (Table I): MS (CI-CH_4) 553 (M + 1, 72), 495 (70), 425 (100), 410 (13), 395 (12), 383 (22), 159 (20) for the *Z* form.

Repeated chromatography of the **12bE–12bZ** mixture gave the pure *Z* isomer as red flakes, mp 62–64 °C. The NMR data are found in Table II: MS (CI-NH_3) 695 (M^+ + 1, 100), 637 (13), 551 (15), 229 (30), 198 (25); high-resolution MS (M^+) found 694.1877, calcd for $C_{31}H_{38}N_2O_{12}S_2$ 694.1888; UV (EtOH) 448 (2900), 340s (6500), 273 (35 000), 240 (28 000).

2,3-Bis(methoxycarbonyl)-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-benzo[*b*]thiopyran-4-thione (19) was obtained as dark green prisms, mp 142–143 °C, after recrystallization from toluene–heptane: ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 6 H), 2.54 (s, 2 H), 2.69 (s, 2 H), 3.85 (s, 3 H), 3.91 (s, 3 H); MS (70 eV) 340 (M^+, 24), 293 (100), 64 (41), 59 (80), 41 (58); high-resolution MS (M^+) found 340.0453, calcd for $C_{15}H_{16}O_5S_2$ 340.0439; UV (EtOH) 426 (4900), 371 (10 600), 268 (7500), 225 (16 600).

2,3,5,6-Tetrakis(methoxycarbonyl)-8*H*-8,8-dimethyl-1,4-dithiaphenalene (23) was obtained as dark brown crystals, mp 148–150 °C, after recrystallization from toluene: ^{1}H NMR ($CDCl_3$) δ 1.12 (s, 6 H), 3.78 (s, 6 H), 3.85 (s, 3 H), 3.86 (s, 3 H), 5.29 (d, 1 H, J = 1.9 Hz), 5.38 (d, 1 H, J = 1.9 Hz); ^{13}C NMR, see Figure 2; MS (16 eV) 464 (M^+, 5), 449 (100), 444 (12), 332 (11), 216 (15), 59 (74); UV (EtOH) 514 (1600), 389 (3250), 287 (18 500), 273s (17 800), 244s (20 800), 205 (27 500); elemental analysis C, H, S.

2,3,5,6-Tetrakis(methoxycarbonyl)-3a-[*N*-methyl-*N*-[2-[*N*′-methyl-*N*′-[bis(methoxycarbonyl)vinyl]amino]ethyl]amino]-3a*H*-7,8-dihydro-8,8-dimethyl-1,4-dithiaphenalene (28) was obtained after chromatographic purification as a brownish solid, mp 70–72 °C. The compound is given the 7H structure, since this has the most extended conjugation, but the tautomeric 9H structure cannot be excluded: ^{1}H NMR ($CDCl_3$) δ 0.92 (s, 3 H), 1.05 (s, 3 H), 2.26 (d, 1 H, J = 14.2 Hz), 2.45 (d, 1 H, J = 14.2 Hz), 2.39 (s, 3 H), 2.88 (s, 3 H), 2.95–3.25 (m, 4 H, ABCD system), 3.60 (s, 3 H), 3.75 (s, 6 H), 3.77 (s, 3 H), 3.83 (s, 3 H), 3.89 (s, 3 H), 4.54 (s, 1 H), 5.40 (s, 1 H); MS (CI-NH_3) 695 (M^+ + 1, 8), 465 (18), 222 (100); UV (EtOH) 492 (1600), 360s (4500), 284 (32 500); CD (EtOH, first eluted enantiomer) 490 (−0.37), 370 (0.94), 305 (−2.01), 257 (6.31), 215 (1.9). The relation between **23** and **28** was confirmed by a TLC experiment, in which a pure sample of **28** was run along the edge of a square plate. Two spots appeared, corresponding to *23* and **28**. The plate was rotated 90° to place the spots along the bottom edge, and the chromatography was repeated. The spot corresponding to **23** moved as a single spot, whereas that due to **28** was again separated into two spots corresponding to **23** and **28**.

Ring Opening of the Spiro Compounds. A solution of **8aE** (0.049 g) in 96% aqueous ethanol (100 mL) with concd HCl (5.8 μL) was kept at ambient temperature, and the UV spectrum was recorded at regular intervals. The successive spectra passed through isosbestic points. When the first reaction had subsided after 18 h, the solution was quenched with excess sodium acetate and evaporated, the residue was extracted with dichloromethane, and the extract was subjected to flash chromatography on silica with toluene–ethyl acetate as the mobile phase. Pure **2,3-bis-**

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(methoxycarbonyl)-4-[*N*-benzyl-*N*-[2-(benzylamino)-ethyl]amino]-5(*E*)-[[1,2-bis(methoxycarbonyl)vinyl]thio]-7,7-dimethyl-7*H*-benzo[*b*]thiopyran (10a*E*) was obtained as a red semisolid material (0.018 g, 37% yield): ^{1}H NMR spectral data are given in Table II; MS (CI-CH_4) 704 (M^+, 57), 434 (100), 295 (75), 145 (72), 91 (60); high-resolution MS (M^+) found 704.2222, calcd for $C_{37}H_{40}N_2O_8S_2$ 704.2226; UV (EtOH) 446 (2100), 340s (5500), 268 (12800), 242 (14000), 204 (35000). When a similar reaction was performed with a solution of 8a*Z* (0.045 g) and concd HCl (5.4 μL) in acetonitrile (300 mL), 10a*Z* was obtained, also as an amorphous red material that could be induced to crystallize (mp 100–102 °C, 0.037 g, 82% yield): MS (CI-CH_4) 704 (M^+, 30), 466 (38), 450 (43), 434 (100), 253 (38); high-resolution MS (M^+) found 704.2239, calcd for $C_{37}H_{40}N_2O_8S_2$ 704.2226; UV (EtOH) 450 (1050), 267 (10200), 245 (11200), 205 (28000).

As discussed previously, a mixture of 10b*E* and 10b*Z* was obtained in the chromatographic workup after the reaction of 5b with DMAD. The yield was as high as 22% in some experiments. These compounds may have been formed in silica-catalyzed ring opening of the spiro compounds 8b*E* and 8b*Z*. Repeated chromatography gave no complete separation, but the NMR spectral data of the individual compounds could be extracted from spectra of the mixtures (Table II): MS (CI-NH_3) 553 (M + 1, 100); high-resolution MS (M^+) found 552.1610, calcd for $C_{25}H_{32}N_2O_8S_2$ 552.1600.

Hydrolysis of 8a*E* and 8a*Z*. In a typical experiment, a solution of 8a*E* (0.070 g) and concd HCl (0.8 μL) in 96% aqueous methanol (100 mL) was left for 52 h at ambient temperature. After evaporation and chromatographic workup as in the previous text, two isomeric compounds $C_{21}H_{22}O_9S_2$ were isolated in quantities of 0.013 and 0.018 g. The NMR spectral data conform with structures 13*E* and 14*E*. Besides, a quantity of 10a*E* was obtained (0.023 g). The hydroxylic proton resonance of 14*E* has not been located, possibly because of exchange with acidic impurities, but the framework of this compound follows from the ^{1}H and ^{13}C NMR spectra and from the observation that a dry sample of 14*E* after standing for some months had been transformed to 13*E*. A similar experiment with 8a*Z* over 48 h gave 13*Z* (25% yield) and 14*Z* (60% yield) together with 10a*Z* (15% yield). **2,3-Bis(methoxycarbonyl)-5(*E*)-[[1,2-bis(methoxycarbonyl)-vinyl]thio]-7,7-dimethyl-7,8-dihydrobenzo[*b*]thiopyran-4-one (13*E*)**: ^{1}H NMR ($CDCl_3$) δ 1.09 (s, 6 H), 2.54 (s, 2 H), 3.72 (s, 3 H), 3.78 (s, 3 H), 3.95 (s, 6 H), 6.03 (s, 1 H), 6.25 (s, 1 H); MS (CI-NH_3) 500 (M^+ + 18, 100), 483 (M^+ + 1, 78), 341 (15), 52 (18); high-resolution MS (M^+) found 482.0701, calcd for $C_{21}H_{22}O_9S_2$ 482.0705. The enol analogue 14*E*: ^{1}H NMR ($CDCl_3$) δ 1.14 (s, 6 H), 3.71 (s, 3 H), 3.79 (s, 3 H), 3.83 (s, 3 H), 3.84 (s, 3 H), 5.43 (d, 1 H, J = 1.8 Hz), 6.23 (d, 1 H, J = 1.8 Hz), 5.95 (s, 1 H); MS (CI-NH_3) 500 (M^+ + 18, 100), 483 (M^+ + 1, 45), 391 (100), 342 (58), 194 (59), 178 (92); high-resolution MS (M^+) found 482.0687, calcd for $C_{21}H_{22}O_9S_2$ 482.0705. 13*Z*: ^{1}H NMR ($CDCl_3$) δ 1.02 (s, 6 H), 2.50 (s, 2 H), 3.74 (s, 6 H), 3.86 (s, 6 H), 5.79 (s, 1 H), 6.57 (s, 1 H); MS (16 eV) 482 (M^+, 100), 92 (68), 56 (59). The 4-hydroxy analogue 14*Z*: ^{1}H NMR ($CDCl_3$) δ 1.09 (s, 6 H), 3.78 (s, 3 H), 3.79 (s, 6 H), 3.85 (s, 3 H), 5.39 (d, 1 H, J = 1.8 Hz), 6.00 (d, 1 H, J = 1.8 Hz), 6.43 (s, 1 H); MS (16 eV) 482 (M^+, 15), 433 (100), 275 (68), 262 (33). In one experiment with 8a*Z* in ethanol over 36 h a 25% yield of the ethoxy derivative 15*Z* was also isolated: ^{1}H NMR ($CDCl_3$) δ 1.09 (s, 6 H), 1.26 (t, 3 H), 3.77 (s, 3 H), 3.79 (s, 6 H), 3.84 (s, 3 H), 3.88 (q, 2 H), 5.38 (d, 1 H, J = 1.9 Hz), 5.99 (d, 1 H, J = 1.9 Hz), 6.43 (s, 1 H); MS (16 eV) 510 (M^+, 30), 495 (100), 339 (15), 335 (22), 101 (23). All compounds 13–15 were obtained as noncrystalline materials. The elemental analyses (C, H, N, S) were accurate to within ± 0.4%.

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectra of 8b*E*, 8b*Z*, 15*Z*, and 28. ^{1}H NMR spectra of 13*Z* and 14*Z*. Tables of ^{13}C NMR chemical shifts for 8a*E*, 8a*Z*, 8b*E*, and 8b*Z* (Table Ib), for 10a*E*, 10a*Z*, 10b*E*, 10b*Z*, and 12b*Z* (Table IIb), and for 19 and 28 (Table V). 2D INADEQUATE spectra of 23 in the ranges δ 117–169 (Figure 3) and 119–127 (Figure 4). Detailed description of INADEQUATE experiments. Tables of fractional atomic positional coordinates and equivalent isotropic displacement coefficients for non-hydrogen atoms (Table III), of physical properties and parameters for data collection and refinement (Table IV), of bond lengths (Table VII), of bond angles (Table VIII), of anisotropic displacement coefficients (Table IX), and of H atom coordinates (Table X). Superpositon of the crystal structures of 8a*E* (- - -) and 8a*Z* (—) (Figure 1a), stereo pictures of 8a*E* (Figure 1b) and 8a*Z* (Figure 1c), and a picture of 8a*Z* with numbers (Figure 1e) (47 pages). Ordering information is given on any current masthead page.

N-Fluorobis[(trifluoromethyl)sulfonyl]imide: An Efficient Reagent for the α-Fluorination of Functionalized Carbonyl Compounds

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The *N*-fluorobis[(trifluoromethyl)sulfonyl]imide (1) has been used in the electrophilic fluorination of the lithium enolate of esters, amides, and ketones. The corresponding α-fluorocarbonyl compounds have been obtained in good yields. The α-fluorination of β-diesters, β-diamides, β-keto esters, and β-diketones has been performed either on the neutral compounds or on the metal enolates. In this way some geminal azafluoro, chlorofluoro, fluorooxy compounds have been prepared in nearly quantitative yields. Also some α-keto esters and acids have been selectively monofluorinated in the β-position by simple treatment of the neutral compound with 1.

Introduction

A fluorine atom is frequently used to replace a hydrogen atom (isosteric substitution) or a hydroxyl group (isopolar substitution) in an organic molecule. This is due to the fact that such a replacement imparts specific and often useful properties to the compound with respect to those of the parent, unfluorinated product. Selectively fluorinated substances are finding increasing applications in analytical,[2] biological,[3] and medicinal chemistry.[4] Re-

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