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Butadienic Building Blocks from 2-Nitrothiophene as Precursors of Nitrogen Heterocycles: Intriguing Dichotomic Behavior[§]

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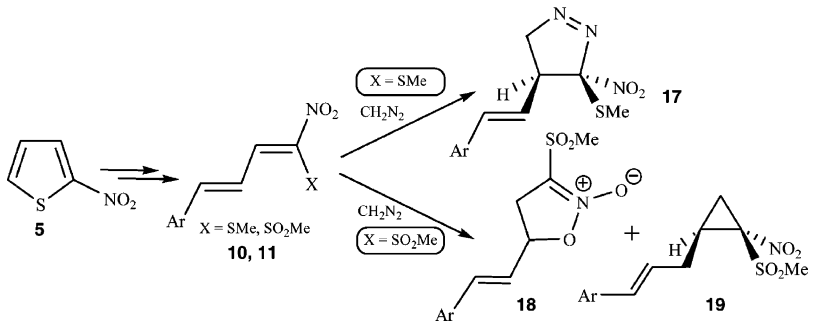

With the goal of their exploitation for the synthesis of heterocycles, sulfides **10** and sulfones **11**, derived from the initial ring-opening of 2-nitrothiophene (**5**) with pyrrolidine/$AgNO_3$ in EtOH, were reacted with diazomethane. Interesting dichotomic behavior was found to yield pyrazolines **17** from **10** and isoxazolines **18** (as the main products) from **11**. Intriguingly enough, in the latter case, an unexpected apparent C−C methylene insertion was also observed, leading to the homologous cyclopropanes **19** as secondary products.

1. Introduction

Within the frame of a long-standing research project aimed at the synthetic exploitation of the versatile butadienic building blocks derived from the ring-opening of nitrothiophenes with secondary amines,[1−3] in the last few years we have reported a number of successful applications of the highly functionalized dinitro- (**3**)[1,2] or nitro-butadienes (**4**)[1,3] obtainable from 3,4-dinitrothiophene[4] or 3-nitrothiophene,[5] respectively (Scheme 1). By means of proper modification of the existing functionalities, both **3** and **4** have actually proven to be effective precursors of linear molecules as well as of homo- or heterocyclic derivatives. The results have significantly widened the field of the synthetic methodologies available, in particular, for access to variously functionalized oxygen and/or nitrogen heterocycles.[1−3]

In 1974, it was reported[1,6] that 2-nitrothiophene (**5**) undergoes ring-opening with secondary amines (Scheme 2), leading to nitrobutadiene disulfides **7** as the result of a fast oxidation of the expected but never isolated thiols **6** (path a in Scheme 2). In the presence of $AgNO_3$, the resulting silver thiolates **8** (path b in Scheme 2) could be conveniently isolated and successively treated with excess MeI, eventually yielding the

[§] This paper is dedicated to the memory of Prof. Carlo Dell'Erba.

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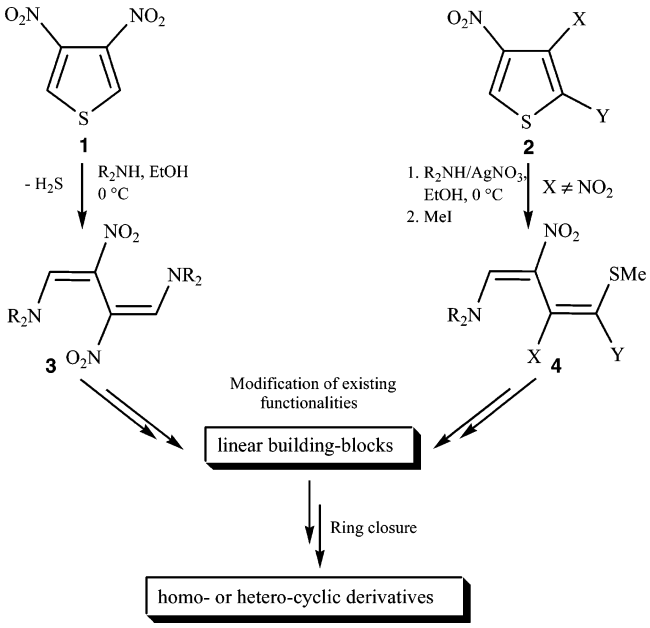
SCHEME 1



4-methylsulfanyl-4-nitro-1,3-butadiene-1-amines **9**. The just-mentioned interesting results obtained from **3** and, more recently, from **4** have conceivably fostered a renewed interest toward the dienes **9** as potential building blocks: the different stereochemical arrangement of the butadiene moiety and the functionalization of the nitro-substituted C atom should enforce original outcomes with respect to molecules such as **3** and/or **4**. In agreement with such expectations, we report herein the attainment of novel, original targets either homo- or heterocyclic in nature following preliminary modifications of the preexisting functionalities of **9**. Such results undoubtedly expand the pool of methodologies available for the synthesis of ring systems (such as cyclopropyl[7] or isoxazole[8] derivatives), whose interest both in organic and in biological chemistry is clearly testified by the large amount of papers published on the subject.

2. Results and Discussion

2.1. Optimization of the Ring-Opening of 2-Nitrothiophene with Pyrrolidine. Our interest in the chemical behavior of **9** has led us first of all to optimize the preparative procedure for a selected aminonitrobutadiene that could represent the best compromise between synthesis and further reactivity. In this respect, **9a** (R_2N = pyrrolidinyl) proved to be the most suited, and its synthesis could be performed one-pot (Scheme 2, and see Experimental Section), without isolation of **8**, raising the yield to a more than satisfactory 80% by means of a proper choice of the reaction conditions. As previously reported,[1,6] the ring-opening resulted to be completely diastereoselective, as **9a** was always obtained exclusively in the 1*E*,3*Z* configuration shown in Scheme 2.

2.2. Synthesis of Aryl-Substituted Butadiene Sulfides 10 and Sulfones 11. The treatment of **9a** in THF at −30 °C with 1.1 molar equiv of a series of aryl Grignard reagents, followed by acidic quenching (Scheme 3), has allowed us to isolate compounds **10a**−**f** in generally high yields (see Table 1). The reaction proved to be completely regioselective (replacement occurring exclusively at the enamino moiety) as well as stereospecific, proceeding with retention of configuration at both C=C double bonds.[5a] Oxidation of the methylthio group of **10a**−**f** with *m*-CPBA in dichloromethane furnished the sulfones **11a**−**f** in high, when not quantitative, yields (Table 1).

2.3. Reactions of the Nitrobutadienic Building Blocks 10 and 11 with Diazomethane. The cycloaddition reaction of electron-deficient alkenes with diazomethane represents a useful access to a number of interesting targets, such as pyrazolines and pyrazoles and/or cyclopropanes, as is supported in the literature.[9] Nitroalkenes are particularly suited in this regard, as the resulting nitrocyclopropanes can be in turn considered important building blocks thanks to the presence of the versatile nitro group.[10] In this context, in the course of a previous study[2b] on the synthetic exploitability of the 1,4-diaryl-2,3-dinitro-1,3-butadienes **12**, easily obtainable by the replacement of the two dialkylamino moieties of **3**,[1] their treatment with diazomethane led (Scheme 4) to the isolation of mono- (**13**, as a single

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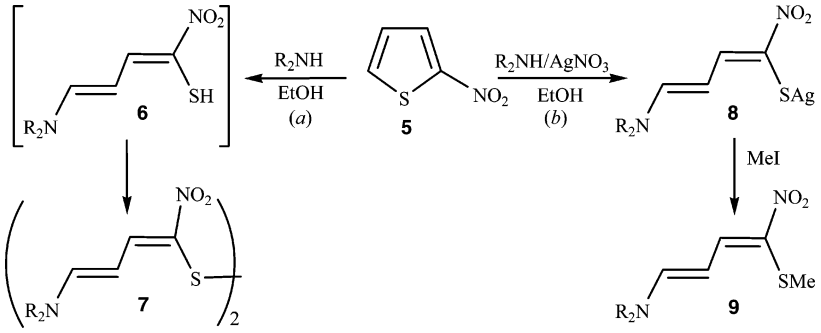
SCHEME 2



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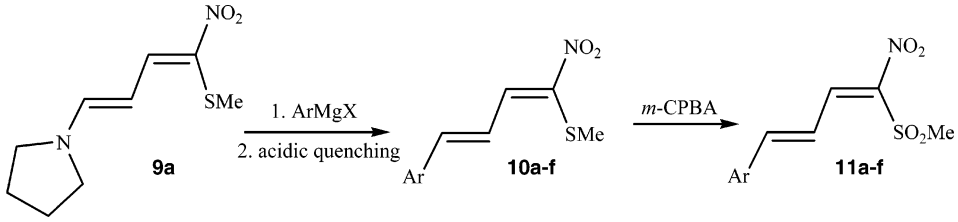

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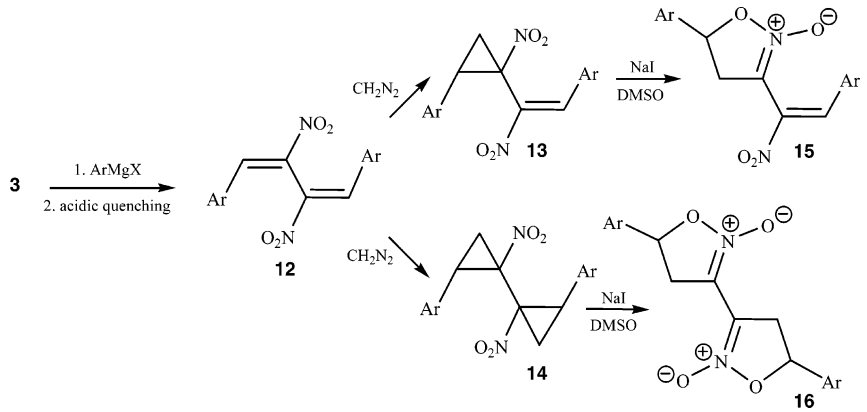


TABLE 1. Synthesis of 10a−f and 11a−f According to Scheme 3

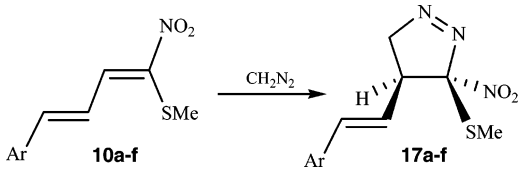
Ar in ArMgX	**10** (yield %)[a]	**11** (yield %)[a]
Ph	**10a** (84)	**11a** (95)
4-MeC_6H_4	**10b** (91)	**11b** (96)
4-MeOC_6H_4	**10c** (92)	**11c** (95)
4-ClC_6H_4	**10d** (78)	**11d** (88)
1-naphthyl	**10e** (85)	**11e** (99)
2-thienyl	**10f** (69)	**11f** (78)

[a] Yield of isolated, pure compound.

diastereoisomer) or bis-cyclopropanes (**14**, as a mixture of a *d,l* and a *meso* form), depending on the reaction conditions. The resulting nitrocyclopropyl moieties of **13** or **14** could be effectively isomerized, in the presence of NaI as the catalyst, to the corresponding cyclic nitronates, yielding **15** and **16**, respectively, which could be further elaborated.[2c]

Herein, nitrosulfides **10a−f** in THF were added with 2 molar equiv of diazomethane at 0 °C, and the reaction mixture was left overnight at room temperature. After removal of the solvent and purification of the crude residue, NMR analysis showed in any instance the formation of a single product, definitively identified as the diastereomerically pure racemic 3-methylsulfanyl-3-nitro-4-styryl-4,5-dihydro-3*H*-pyrazole **17** (Scheme 5) by means of a single-crystal X-ray analysis on the model **17a**

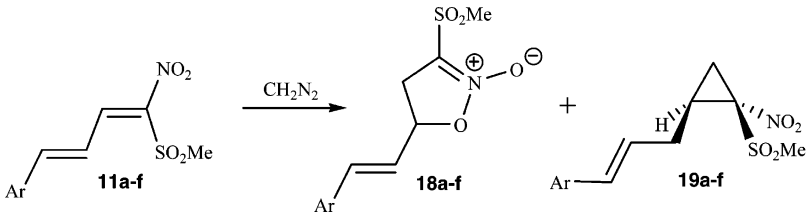
SCHEME 5



(see the ORTEP representation in the Supporting Information). Yields of **17a−f** are reported in Table 2 and are satisfactory.

Interestingly enough, as mentioned previously, our prior experience on the reactivity of diazomethane with nitroolefins led to the direct isolation of cyclopropanation derivatives (**13** or **14**); no evidence was ever found for the intermediacy of pyrazoline precursors, although their initial formation followed by fast nitrogen extrusion at room temperature cannot be excluded. The result herein is on the contrary in agreement with literature data,[9] which usually testify for the formation of isolable pyrazolines. As expected for a 1,3-dipolar cycloaddition, the reaction is completely stereospecific: the original *cis*/*trans* relationships of the substituents in **10** are maintained in **17**, and accordingly, **17a−f** are diastereomerically pure racemic mixtures. Furthermore, the cycloaddition also proves to be regioselective, involving exclusively the nitrovinyl double bond of the starting diene system.

SCHEME 6



SCHEME 7

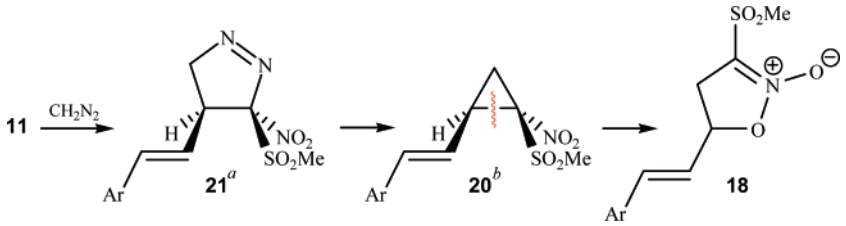


TABLE 2. Treatment of Sulfides 10 or Sulfones 11 with Diazomethane:[a] Yields of Pyrazolines 17 (Scheme 5), Isoxazoline *N*-Oxides 18, and Cyclopropanes 19 (Scheme 6)[b]

Ar	**17** (yield %)[c]	**18** (yield %)	**19** (yield %)[c]
Ph	**17a** (80)	**18a** (44)	**19a** (31)
4-MeC_6H_4	**17b** (83)	**18b** (65)	**19b** (25)
4-$MeOC_6H_4$	**17c** (76)	**18c** (50)	**19c** (34)
4-ClC_6H_4	**17d** (71)	**18d** (54)	**19d** (20)
1-naphthyl	**17e** (73)	**18e** (64)	**19e** (24)
2-thienyl	**17f** (82)	**18f** (64)	**19f** (27)

[a] CH_2N_2: 2 molar equiv, THF, 0 °C to rt, 15 h. [b] Yields of isolated, pure compounds. [c] Isolated as single racemic diastereoisomers.

When we applied to nitrosulfones **11a−f** the same reaction conditions employed for the nitrosulfides **10** (2 molar equiv of diazomethane at 0 °C, then overnight at room temperature (rt)), the outcome was, at a first sight, completely different: the isoxazoline *N*-oxides **18a−f** (Scheme 6) were isolated as the main products, always accompanied by minor quantities of the cyclopropane derivatives **19a−f**, according to the data reported in Table 2.

As far as the isoxazolines **18** are concerned, their formation may be explained on the grounds of the already cited well-known nitrocyclopropane to five-membered cyclic nitronate isomerization (Scheme 7 and cf. Scheme 4).[11] Such a process may be usually induced by thermal activation,[11a] or by electrophilic[11a] or nucleophilic catalysis,[11b,c] and proceeds through the selective breakage of the most substituted bond of the cyclopropane ring. Actually, when the reaction was performed on **11d** (Ar = 4-ClC_6H_4), the yellow oil **20d** was isolated, whose ^1H and ^{13}C NMR signals were in agreement with the cyclopropanation of the nitrovinyl moiety (see Experimental Section); during the chromatographic purification, this underwent extensive isomerization to the corresponding isoxazoline *N*-oxide **18d**. Also, for **11b** (Ar = 4-MeC_6H_4) and **11e** (Ar = 1-naphthyl), the ^1H NMR analysis of the crude final reaction mixture showed the presence of signals most likely attributable to a cyclopropyl derivative **20**, which isomerized during the workup to the corresponding isoxazoline *N*-oxide (**18b** and **18e**, respectively). Thus, it seems most likely that a fast isomerization to the isolated compounds **18** follows the preliminary formation of cyclopropanes **20** (Scheme 7). Such a fast **20** to **18** isomerization easily could find its rationale in the contemporaneous presence of two strongly electron-withdrawing groups on the same carbon atom of the cyclopropyl ring: we can reasonably suppose that these substituents would favor the heterolytic C(1)−C(2) bond breakage involved by means of both a strong polarization and an effective delocalization of the negative charge developing on the tertiary C(2) carbon.

Concomitantly, the incipient positive charge on the secondary C(1) carbon would be in turn stabilized by the conjugative effect exerted by the styrene moiety. Furthermore, as our reaction conditions seem hardly compatible with the existence of singlet or triplet carbene,[12] we can reasonably speculate that, when reacted with diazomethane, sulfones **11** herein undergo, analogously to sulfides **10**, a 1,3-dipolar cycloaddition, to give the unstable, never observed pyrazolines **21** (Scheme 7 and cf. Scheme 5). From these, nitrogen extrusion would lead to **20**.

The presence, in the conditions described, of the homologous cyclopropyl derivative **19** (Scheme 6), isolated throughout in 20−34% yield as a single racemic diastereomer (Table 2), deserves some further comment. The structures of such unexpected products were deduced on the grounds of ^1H and ^{13}C NMR analysis. Thus, in the case of **19a**, the presence of an allylic moiety was confirmed by the observation that the two vinyl protons exhibit two doublets of triplets at δ 6.25 (J 15.9 and 6.3 Hz) and 6.51 (J 15.9 and 1.5 Hz). Moreover, NOE experiments performed on **19a** and **19b** showed that the allylic methylene is *cis* to the methylsulfonyl group; in particular, when irradiating the methylsulphonyl protons of **19b**, the only appreciable, although small (ca. 0.60%) NOE detectable was the one relevant to such methylene protons.

It should be noted that the cyclopropyl ring of **19** does not spontaneously isomerize into the corresponding isoxazoline *N*-oxide, well in agreement with the occurrence that, in this case, the breakage of the C(1)−C(2) cyclopropane bond would develop a positive charge on a carbon atom in a nonconjugated position.

The formation of **19** from **11** formally requires both a methylene insertion within a C−C single bond and cyclopro-

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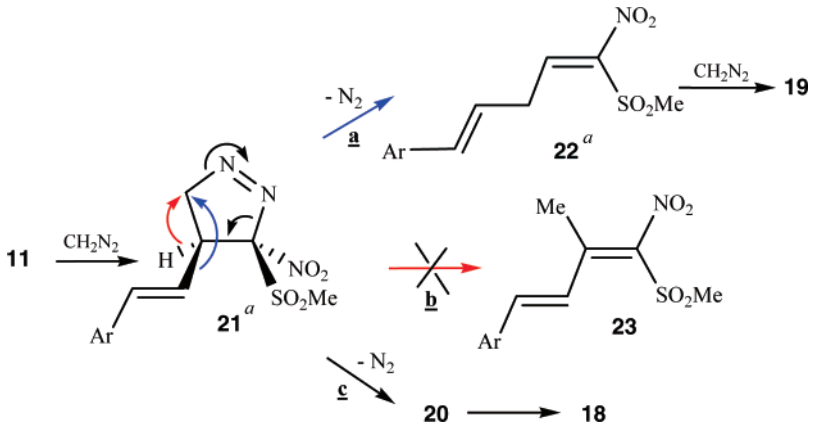
SCHEME 8



panation of the nitrovinyl moiety. The methylene insertion surely precedes the cyclopropane formation because the treatment of the only isolable cyclopropane derivative **20d** with diazomethane did not lead to any appreciable formation of **19d**. We can reasonably assume that **19** is derived from the reaction of diazomethane with the (never detected) nitroalkene precursor **22** (Scheme 8). The formation of the latter can be in turn justified by means of nitrogen extrusion (Scheme 8, black arrows) from **21** coupled with the interesting migration of a styrene moiety from C(4) to C(5) of the pyrazoline nucleus (blue arrow: path a in Scheme 8).

Although unprecedented, to our knowledge, in the pyrazoline chemistry, such an occurrence finds some tight analogies in previous reports on the migration of aryl moieties in a similar context.[13,14] On the other hand, at least in a different system, a higher migrating aptitude of styryl versus phenyl toward an adjacent positively charged C atom has been acknowledged for long time.[15]

Interestingly enough, no definite evidence for a hydride 1,2-shift (which would lead to the isomer **23**; see red arrow in Scheme 8: path b) has been collected, notwithstanding that its occurrence is more frequently reported within the thermal decomposition of pyrazolines;[14,16,17] such an outcome can be tentatively rationalized on conformational grounds, assuming for the styryl moiety a pseudo-equatorial position, reportedly more favorable for the 1,2-shift to be performed.[13]

Well in agreement with the pivotal role assigned to the pyrazoline **21** in directing the reaction toward the eventual formation of either **18** (Schemes 7 and 8, path c) or of **19** (Scheme 8, path a), the competition of the styryl migration versus cyclopropane ring formation is sizeably favored, as already noticed,[13] by electron-donating aryl substituents (34 vs 20% yield of **19** for Ar = 4-$MeOC_6H_4$ and 4-ClC_6H_4, respectively: cf. Table 2).

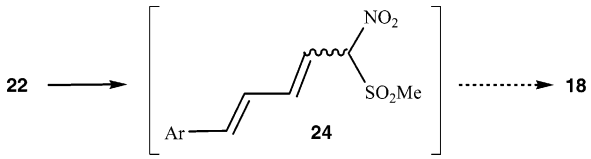
A further interesting facet of the system under examination is unveiled by the results reported in Table 3, relevant to runs carried out at different diazomethane/substrate ratios on the model nitrosulfone **11c**. Actually, as expected on the grounds of the proposed reaction scheme and of the nature of the isolated final cyclopropyl derivatives **19** (whose structure requires the uptake of two CH_2 moieties), entries 1−3 in Table 3 clearly show that the yield of **19c** levels off above a 2:1 reactant/substrate molar ratio. On the other hand, in the case of a lower diazomethane to **11c** ratio (Table 3, entry 4), the foreseable significant decrease of the yield of **19c** is accompanied by a sizable increase in that of the isoxazoline derivative **18c**. Such a result, which encompasses the evident practical advantage of allowing significant optimization of the yield of **18** bypassing the concurrent formation of **19**, is justifiable within Scheme 8 only when admitting that, following the competitive, irreversible transformation of the common intermediate **21** into **20** and **22**, the latter (or a derivative) can convert into **18** in the case of the absence of residual diazomethane in the reaction mixture. Given its synthetic and mechanistic implications, this particular aspect of the reactivity of nitrosulfones **11**, which does not influence the main conclusions herein, is presently under further investigation. Thus far, we can only hypothesize a thermodynamically favored isomerization (Scheme 9) of the surviving alleged 1,4-butadiene **22** to the conjugated tautomer **24**, which seems a more reasonable candidate for the conversion into **18**.

TABLE 3. Results from Treatment of Sulfone 11c with Diazomethane[a] at Different CH_2N_2/Substrate Molar Ratios

entry	CH_2N_2/**11c** molar ratio	**18c** (yield %)[b]	**19c** (yield %)[b]
1[c]	10:1	48	30
2[c]	5:1	51	35
3	2:1	50	34
4[d]	1.2:1	83	14

[a] THF, 0 °C to rt, 15 h if not otherwise specified. [b] Yields of isolated compounds. [c] Reaction time: 3 h. [d] Identical results were obtained by reducing the reaction time to 3 h.

SCHEME 9



3. Conclusion

The present study represents a further significant advancement in exploitation of the ring-opening of nitrothiophenes as a means to provide polyfunctionalized building blocks. As a first

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breakthrough inside the potential applications of the nitrodienamine **9a**, the replacement of the pyrrolidine moiety with aryl Grignard reagents is high-yielding, regioselective, and stereospecific. The resulting (methylthio)nitrobutadienes **10** and their oxidation products **11** have in turn proved to be valuable intermediates toward a number of homocycles as well as nitrogen and/or oxygen heterocycles following an initial, completely regio- and stereoselective 1,3-dipolar addition of diazomethane onto the nitrovinyl moiety. Interestingly enough, the final outcome of the reaction dramatically depends on the stability, in the reaction conditions, of the alleged primarily formed pyrazolines (**17** and **21** from **10** and **11**, respectively) and hence on the nature of the substituents present in the butadiene system. In this respect, the oxidation level of the sulfur atom geminal to the nitro group seems to play a decisive role. From a mechanistic point of view, the 1,2-styryl migration eventually leading to **19** surely represents an interesting behavior of pyrazolines **21**. It should be remarked that 2-nitrothiophene is quite peculiar in providing, via ring-opening and successive transformations, a 1,3-butadiene moiety possessing two geminal strongly electron-withdrawing groups such as NO_2 and SO_2R: a structural feature that is surely bound to characterize the chemical behavior of building blocks such as **11**. Thanks to the embedded functionalities, the heterocyclic (**17** and **18**) as well as homocyclic (**19**) derivatives isolated herein should in turn be regarded as intermediates of potentially valuable interest toward the synthesis of, for example, isoxazoles and their ring-opening products.

4. Experimental Section

4.1. Ring-Opening of 2-Nitrothiophene with Pyrrolidine and Silver Nitrate. The reaction of 2-nitrothiophene **5** with some secondary amines and silver nitrate in absolute ethanol has been previously described.[6] In our optimized conditions, pyrrolidine (5.0 g, 70.3 mmol) was added dropwise to a solution of $AgNO_3$ (1.5 g, 8.83 mmol) in ethanol (30 mL). Then, 2-nitrothiophene (1.0 g, 7.75 mmol) in ethanol (30 mL) was added, and immediately a dark-red precipitate was obtained. The resulting suspension was kept at rt in the dark for ca. 3 days and then treated with excess methyl iodide. After the standard workup, column chromatography over silica gel (petroleum ether/diethyl ether gradients as eluent) allowed isolation of 80% of the ring-opening product **9a**. (1*E*,3*Z*)-1-(4-Methylsulfanyl-4-nitrobuta-1,3-dienyl)pyrrolidine (**9a**): (1.331 g, 80%). Red solid, mp 135.4−136.5 °C (ethanol); ^{1}H NMR ($CDCl_3$) δ 1.93−2.14 (4H, m), 2.24 (3H, s), 3.40 (2H, app s), 3.61 (2H, app t), 5.60 (1H, t, *J* 12.5 Hz), 7.35 (1H, d, *J* 12.0 Hz), 8.25 (1H, d, *J* 12.6 Hz); ^{13}C NMR (CDCl3) δ 17.3, 25.0, 47.6, 52.9, 98.2, 129.8, 149.0, 152.9 (two carbons are accidentally isochronous). Anal. Calcd for $C_9H_{14}N_2O_2S$ (214.28): C, 50.45; H, 6.59; N, 13.07%. Found: C, 50.37; H, 6.61; N, 13.00%.

4.2. Reactions of 9a with Aromatic Organometallic Reagents. To a suspension of 1-(4-methylsulfanyl-4-nitrobuta-1,3-dienyl)-pyrrolidine (**9a**; 1.0 g, 4.67 mmol) in THF (55 mL), cooled to −30 °C, the organometallic reagent (1.1 molar equiv) in THF or Et_2O was slowly added under argon by syringe. The reaction mixture was kept under stirring for 20 min (the end of the reaction being judged by TLC analysis) and eventually poured into a dichloromethane/ice/HCl (1.1 molar equiv) mixture. After separation of the two layers, the aqueous phase was extracted with dichloromethane, and the collected organic extracts were washed with water and dried over Na_2SO_4. Concentration under vacuum of the extracts gave a crude product that was purified by column chromatography over silica gel (petroleum ether/dichloromethane gradients as eluent). Yields of compounds **10a**−**f** are collected in Table 1.

4.2.1. 1-Methyl-4-[(1*E*,3*Z*)-(4-methylsulfanyl-4-nitrobuta-1,3-dienyl)]benzene (10b). (1.000 g, 91%). Yellow solid, mp 99.6−100.1 °C (petroleum ether); ^{1}H NMR ($CDCl_3$) δ 2.39 (6H, two partially overlapped s), 7.14−7.35 [4H in all, partially overlapped dd (*J* 15.6 and 10.5 Hz) and m], 7.48 (2H, d, *J* 8.1 Hz), 8.13 (1H, d, *J* 10.5 Hz); ^{13}C NMR ($CDCl_3$) δ 18.1, 21.6, 122.4, 128.1, 129.8, 132.9, 141.1, 142.7, 146.4, 146.6; GC-MS: R_t 13.35, *m*/*z* 235 (M^+). Anal. Calcd for $C_{12}H_{13}NO_2S$ (235.30): C, 61.25; H, 5.57; N, 5.95%. Found: C, 61.21; H, 5.45; N, 5.87%.

4.2.2. 1-Chloro-4-[(1*E*,3*Z*)-(4-methylsulfanyl-4-nitrobuta-1,3-dienyl)]benzene (10d). (0.931 g, 78%). Yellow solid, mp 73.6−74.3 °C (petroleum ether); ^{1}H NMR ($CDCl_3$) δ 2.40 (3H, s), 7.15 (1H, d, *J* 15.3 Hz), 7.31 (1H, dd, *J* 15.3 and 10.8 Hz), 7.38 (2H, br d, *J* 8.6 Hz), 7.51 (2H, br d, *J* 8.6 Hz), 8.10 (1H, d, *J* 10.8 Hz); ^{13}C NMR ($CDCl_3$) δ 18.1, 123.8, 129.1, 129.3, 134.0, 136.2, 141.7, 144.4, 147.7; GC-MS: R_t 13.83, *m*/*z* 255 (M^+). Anal. Calcd for $C_{11}H_{10}ClNO_2S$ (255.72): C, 51.66; H, 3.94; N, 5.48%. Found: C, 51.70; H, 3.85; N, 5.36%.

4.3. Oxidation of Sulfides 10a−f to Sulfones 11a−f. Oxidations were performed with 2 mmol of substrate, according to conditions already described.[3b] After the workup, a crude residue was obtained, generally pure by ^{1}H NMR analysis. Compounds **11** were crystallized in the cold to avoid stereomutation, as was noticed (although not further investigated) in some instances. Relevant yields are reported in Table 1.

4.3.1. 1-[(1*E*,3*Z*)-(4-Methanesulfonyl-4-nitrobuta-1,3-dienyl)]-4-methylbenzene (11b). (0.513 g, 96%). Yellow solid, mp 163.0−163.7 °C (petroleum ether/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 2.41 (3H, s), 3.42 (3H, s), 7.25 (2H, d, *J* 8.3 Hz), 7.40 (1H, d, *J* 15.3 Hz), 7.54 (2H, d, *J* 8.3 Hz), 8.01 (1H, dd, *J* 15.3 and 12.2 Hz), 8.28 (1H, d, *J* 12.2 Hz); ^{13}C NMR ($CDCl_3$) δ 21.8, 44.9, 118.5, 129.5, 130.0, 132.0, 143.4, 143.5, 147.1, 155.8; GC-MS: R_t 14.46, *m*/*z* 267 (M^+). Anal. Calcd for $C_{12}H_{13}NO_4S$ (267.30): C, 53.92; H, 4.90; N, 5.24%. Found: C, 53.72; H, 4.89; N, 5.12%.

4.3.2. 1-Chloro-4-[(1*E*,3*Z*)-(4-Methanesulfonyl-4-nitrobuta-1,3-dienyl)]benzene (11d). (0.506 g, 88%). Yellow solid, mp 208.4−209.5 °C (petroleum ether/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 3.43 (3H, s), 7.35 (1H, d, *J* 15.2 Hz), 7.43 (2H, d, *J* 8.4 Hz), 7.57 (2H, d, *J* 8.4 Hz), 8.03 (1H, dd, *J* 15.2 and 12.0 Hz), 8.26 (1H, d, *J* 12.0 Hz); ^{13}C NMR (CDCl3) δ 45.0, 119.9, 129.7, 130.4, 133.1, 138.4, 143.3, 146.0, 153.3; GC-MS: R_t 14.84, *m*/*z* 287 (M^+). Anal. Calcd for $C_{11}H_{10}Cl\,NO_4S$ (287.72): C, 45.92; H, 3.50; N, 4.87%. Found: C, 45.84; H, 3.49; N, 4.80%.

4.4. Reaction of Compounds 10a−f and 11a−f with Diazomethane. The substrate (1 mmol) was dissolved in dry THF (38 mL) and cooled to 0 °C; diazomethane (2 mmol) in ether was added, and the reaction mixture was left to reach room temperature and kept overnight under magnetic stirring. At the end of the reaction, evaporation of the solvent under reduced pressure yielded a crude residue, which was purified by chromatography over silica gel (petroleum ether/ethyl acetate gradients as eluent). While compounds **17** were the sole reaction products from **10**, when starting from **11**, both **18** and **19** (as a secondary product) were always obtained. Yields of compounds **17**−**19** are reported in Table 2.

4.4.1. (*E*) (3*S*,4*S*)- and (3*R*,4*R*)-4-[2-(4-Methylphenyl)vinyl]-3-methylsulfanyl-3-nitro-4,5-dihydro-3H-pyrazole (17b). (0.229 g, 83%). Pale yellow solid, mp 79.7−80.6 °C (taken up with petroleum ether); ^{1}H NMR ($CDCl_3$) δ 2.34 (3H, s), 2.51 (3H, s), 3.48 (1H, q, *J* 8.4 Hz), 4.47 (1H, dd, *J* 18.0 and 7.8 Hz), 5.16 (1H, dd, *J* 18.0 and 8.4 Hz), 5.89 (1H, dd, *J* 15.6 and 8.4 Hz), 6.54 (1H, d, *J* 15.6 Hz), 7.13 (2H, d, *J* 8.1 Hz), 7.25 (2H, d, *J* 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 13.0, 21.2, 47.0, 81.8, 118.8, 126.5, 128.1, 129.4, 132.8, 137.0, 138.6; GC-MS: R_t 13.25, *m*/*z* 249 ($M^+ - 28$). Anal. Calcd for $C_{13}H_{15}N_3O_2S$ (277.34): C, 56.30; H, 5.45; N, 15.15%. Found: C, 56.19; H, 5.34; N, 15.20%.

4.4.2. (*E*) (3*S*,4*S*)- and (3*R*,4*R*)-4-[2-(4-Chlorophenyl)vinyl]-3-methylsulfanyl-3-nitro-4,5-dihydro-3H-pyrazole (17d). (0.202 g, 71%). Pale yellow solid, mp 57.9−58.8 °C (taken up with petroleum ether); ^{1}H NMR ($CDCl_3$) δ 2.53 (3H, s), 3.49 (1H, q, *J*

8.4 Hz), 4.47 (1H, dd, *J* 18.0 and 8.1 Hz), 5.17 (1H, dd, *J* 17.7 and 7.8 Hz), 5.93 (1H, dd, *J* 15.9 and 8.7 Hz), 6.54 (1H, d, *J* 15.9 Hz), 7.24−7.34 (4H, m); ^{13}C NMR ($CDCl_3$) δ 12.9, 46.8, 81.6, 120.6, 127.7, 127.8, 128.9, 134.0, 134.2, 135.8; GC-MS: R_t 13.77, *m*/*z* 269 ($M^+ - 28$). Anal. Calcd for $C_{12}H_{12}ClN_3O_2S$ (297.76): C, 48.40; H, 4.06; N, 14.11%. Found: C, 48.27; H, 4.05; N, 14.12%.

4.4.3. (*E*) 3-Methanesulfonyl-5-[2-(4-methylphenyl)vinyl]-4,5-dihydroisoxazole 2-Oxide (18b). (0.183 g, 65%). Pale yellow solid, mp 107.1−108.3 °C (petroleum ether/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 2.36 (3H, s), 3.28 (3H, s), 3.40 (1H, dd, *J* 17.1 and 8.4 Hz), 3.70 (1H, dd, *J* 16.8 and 9.3 Hz), 5.45 (1H, q, *J* 8.4 Hz), 6.20 (1H, dd, *J* 15.9 and 7.8 Hz), 6.74 (1H, d, *J* 15.9 Hz), 7.17 (2H, d, *J* 8.1 Hz), 7.31 (2H, d, *J* 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 21.3, 35.9, 40.7, 78.7, 117.0, 121.5, 127.0, 129.5, 132.0, 136.6, 139.3; ESI-MS: *m*/*z* 282.1 [$M + H^+$]. Anal. Calcd for $C_{13}H_{15}NO_4S$ (281.33): C, 55.50; H, 5.37; N, 4.98%. Found: C, 55.47; H, 5.23; N, 5.04%.

4.4.4. (*E*) 5-[2-(4-Chlorophenyl)vinyl]-3-methanesulfonyl-4,5-dihydroisoxazole 2-Oxide (18d). (0.163 g, 54%). Pale yellow solid, which gradually carbonized with heating; ^{1}H NMR ($CDCl_3$) δ 3.28 (3H, s), 3.40 (1H, dd, *J* 16.8 and 8.1 Hz), 3.70 (1H, dd, *J* 16.8 and 9.3 Hz), 5.45 (1H, qd, *J* 8.4 and 0.9 Hz), 6.23 (1H, dd, *J* 15.9 and 7.5 Hz), 6.73 (1H, dd, *J* 15.9 and 0.9 Hz), 7.30−7.39 (4H, m); ^{13}C NMR ($CDCl_3$) δ 35.9, 40.7, 78.0, 116.8, 123.3, 128.2, 129.1, 133.3, 135.0, 135.1; ESI-MS: *m*/*z* 302.1 [$M + H^+$]. Anal. Calcd for $C_{12}H_{12}ClNO_4S$ (301.75): C, 47.76; H, 4.01; N, 4.64%. Found: C, 47.61; H, 4.00; N, 4.55%.

4.4.5. (*E*) (1*R*,2*S*)- and (1*S*,2*R*)-1-[3-(2-Methanesulfonyl-2-nitrocyclopropyl)propenyl]-4-methylbenzene (19b). (0.074 g, 25%). Yellow oil; ^{1}H NMR ($CDCl_3$) δ 2.15−2.27 (1H, m), 2.34 (3H, s), 2.42−2.58 (2H, m), 2.81 (2H, t, *J* 6.3 Hz), 3.39 (3H, s), 6.17 (1H, dt, *J* 15.9 and 6.3 Hz), 6.47 (1H, d, *J* 15.9 Hz), 7.13 (2H, d, *J* 7.8 Hz), 7.24 (2H, d, *J* 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 20.6, 21.1, 29.6, 35.0, 43.4, 81.7, 124.6, 126.0, 129.4, 132.5, 133.6, 137.7; GC-MS: R_t 14.49, *m*/*z* 295 (M^+). Anal. Calcd for $C_{14}H_{17}NO_4S$ (295.35): C, 56.93; H, 5.80; N, 4.74%. Found: C, 56.78; H, 5.86; N, 4.74%.

4.4.6. (*E*) (1*R*,2*S*)- and (1*S*,2*R*)-1-Chloro-4-[3-(2-methanesulfonyl-2-nitrocyclopropyl)propenyl]benzene (19d). (0.063 g, 20%). Colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.15−2.31 (1H, m), 2.44−2.59 (2H, m), 2.83 (2H, t, *J* 6.0 Hz), 3.39 (3H, s), 6.21 (1H, dt, *J* 15.9 and 6.3 Hz), 6.47 (1H, d, *J* 15.9 Hz), 7.24−7.32 (4H, m); ^{13}C NMR ($CDCl_3$) δ 20.9, 29.6, 34.8, 43.5, 81.7, 126.4, 127.4, 128.9, 131.6, 133.5, 134.9; ESI-MS: *m*/*z* 313.8 [M − H]−. Anal. Calcd for $C_{13}H_{14}ClNO_4S$ (315.77): C, 49.45; H, 4.47; N, 4.44%. Found: C, 49.48; H, 4.46; N, 4.38%.

4.4.7. (*E*) (1*S*,2*S*)- and (1*R*,2*R*)-1-Chloro-4-[2-(2-methanesulfonyl-2-nitrocyclopropyl)vinyl]benzene (20d). A yellow oil of satisfactory purity was recovered by fast column chromatography; **20d** underwent extensive conversion to **18d** on silica gel. ^{1}H NMR ($CDCl_3$) δ 2.53 (1H, dd, *J* 9.6 and 7.2 Hz), 2.76 (1H, dd, *J* 10.2 and 7.2 Hz), 3.06 (1H, app q, *J* 9.9 Hz), 3.29 (3H, s), 6.18 (1H, dd, *J* 15.9 and 9.3 Hz), 6.79 (1H, d, *J* 15.9 Hz), 7.27−7.35 (4H, m); ^{13}C NMR ($CDCl_3$) δ 20.7, 38.0, 42.3, 81.9, 121.0, 127.8, 129.1, 133.8, 134.6, 137.2. The low stability of the product prevented a full (microanalysis and/or mass spectroscopy) characterization.

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Supporting Information Available: General experimental methods and characterization data of **10**, **11**, **17**, **18**, and **19a**,**c**,**e**,**f**; ^{1}H NMR spectra for all new compounds; ORTEP, X-ray crystallography, and crystallographic data for **17a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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