Thermal Rearrangement of Nitrone and Nitrile Oxide Cycloadducts to Bicyclopropylidene.[1] Synthesis of 3-Spirocyclopropane-4-pyridone and Furo[2,3-*c*]pyridine Derivatives[†]

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Received October 12, 1995[⊗]

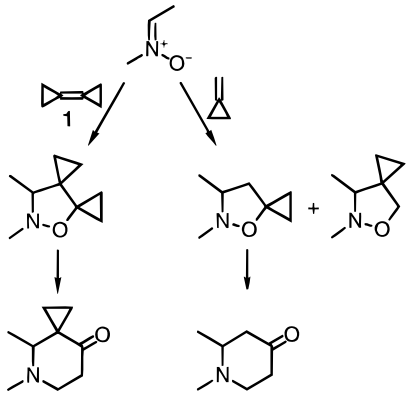
Bicyclopropylidene smoothly undergoes 1,3-dipolar cycloadditions to nitrones or nitrile oxides under different reaction conditions. The strained bisspirocyclopropanated isoxazolidines obtained from nitrones easily rearrange upon heating with selective opening of one of the two spirofused cyclopropane rings. This process produces 4-pyridone, 7-indolizinone, and 2-quinolizinone derivatives containing a spirocyclopropane moiety in the α-position to the carbonyl group in good yields. The same sequence of cycloaddition and rearrangement can be achieved in a "one-pot" operation with considerable benefit for the reaction yield. Bisspirocyclopropaneisoxazolines obtained from nitrile oxides are more stable than their saturated counterparts and rearrange only at higher temperature less chemoselectively. Opening of both spiro-fused cyclopropyl rings followed by aromatization produces interesting 2-substituted dihydrofuro[2,3-*c*]pyridine derivatives.

Introduction

The synthetic methodology based on nitrone and nitrile oxide cycloadditions to methylenecyclopropane followed by thermal rearrangement of the resulting adducts to give a functionalized pyridone (Scheme 1)[2] has already been demonstrated as a useful and versatile strategy to obtain structurally differentiated azaheterocycles, including alkaloids in racemic[3] and nonracemic[4] form.

The choice of bicyclopropylidene (BCP, **1**) as a dipolarophile in the same process appeared particularly interesting, in order to expand the synthetic utility of this methodology. BCP is a uniquely strained tetrasubstituted alkene,[5] which has shown an unusually high reactivity toward electron-deficient cycloaddends.[6] This is a consequence of the electronic properties of its symmetrically substituted double bond, which is significantly shorter than a regular C(sp^2)═C(sp^2) bond, and can be considered to resemble the central bond in butatriene to a certain extent.[7] A recently developed new synthesis of BCP[8] has made this dipolarophile easily available in large enough quantities for synthetic purposes. Albeit BCP has been successfully used in [2 + 2] and [2 + 4] cycloadditions,[2d,6] no reaction with 1,3-dipoles has been reported so far, apart from its oxidation with ozone.[6a]

Scheme 1



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† Dedicated to Professor Nikolai Zefirov on the occasion of his 60th birthday.

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⊗ Abstract published in *Advance ACS Abstracts,* February 1, 1996.

(1) Part 13 in the series Rearrangement of Isoxazoline 5-Spiro Derivatives. Part 12: Brandi, A.; Cicchi, S.; Cordero, F. M.; Frignoli, R.; Goti, A.; Picasso, S.; Vogel, P. *J. Org. Chem.* **1995**, *60*, 6806. This paper is also to be considered as part 34 in the series Cyclopropyl Building Blocks for Organic Synthesis. Part 33: Chaplinski, V.; de Meijere, A. *Angew. Chem.*, in press; *Angew. Chem., Int. Ed. Engl.*, in press.

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(5) (a) Le Perchec, P.; Conia, J.-M. *Tetrahedron Lett.* **1970**, 1587. (b) Fitjer, L.; Conia, J.-M. *Angew. Chem.* **1973**, *85*, 347; *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 332. (c) Schmidt, A. H.; Schirmer, U.; Conia, J.-M. *Chem. Ber.* **1976**, *109*, 2588.

(6) (a) de Meijere, A.; Erden, I.; Weber, W.; Kaufmann, D. *J. Org. Chem.* **1988**, *53*, 152. (b) de Meijere, A.; Wenck, H.; Seyed-Mahdavi, F.; Viehe, H. G.; Gallez, V.; Erden, I. *Tetrahedron* **1986**, *42*, 1291. (c) Weber, W.; de Meijere, A. *Synth. Commun.* **1986**, *16*, 837.

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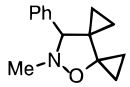
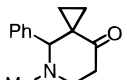
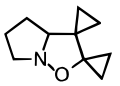
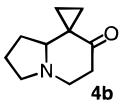
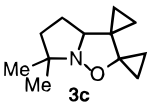
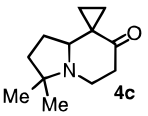
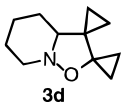
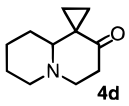
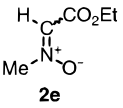
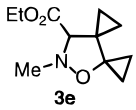
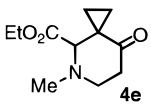
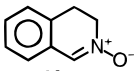
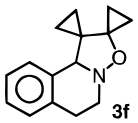
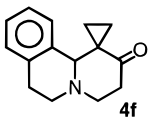
Table 1. Cycloadditions of Nitrones 2a–f to 1 and Thermal Rearrangements of Isoxazolidines 3a–f

Entry	Nitrone	Reaction Conditions	Cycloadduct	Yield (%)	Reaction Conditions	Product	Yield in rearrangement (%)	Yield of "one pot" reaction (calculated for two steps) (%)
1	 **2a**	C_6H_6, 60 °C, 30 d	 **3a**	93	C_6H_5Me, 110 °C, 5 d	 **4a**	63	61 (58)
2	 **2b**	C_6H_6, r. t., 20 d	 **3b**	42	$C_6H_4Me_2$, 125 °C, 11 h	 **4b**	60	–[a] (25)
3	 **2c**	C_6H_6, r. t., 7 d	 **3c**	80	C_6H_6, 80 °C, 7 d	 **4c**	76	80 (61)
4	 **2d**	C_6H_6, 60 °C, 7 d	 **3d**	37	$C_6H_4Me_2$, 125 °C, 6 d	 **4d**	68	48 (25)
5	 **2e**	THF, r. t., 16 d	 **3e**	79	C_6H_5Me, 110 °C, 4 d	 **4e**	61	54 (48)
6	 **2f**	C_6H_6, r. t., 10 d	 **3f**	73	$C_6H_4Me_2$, 125 °C, 5 d	 **4f**	50	73 (36)

[a] The one-pot procedure failed in this case.

The use of an olefin such as BCP (**1**), with its symmetrically substituted double bond, in our methodology avoids any regiochemical problem in the cycloaddition step (Scheme 1).[2] Moreover, the presence of the added cyclopropane ring, which is expected to survive the rearrangement conditions, spiro-fused α to the carbonyl group in the final azaheterocycles, might open new pathways for further and useful synthetic elaborations of the piperidone skeleton.

We report here on the cycloadditions of six nitrones **2a–f** and four nitrile oxides **13a–d** to **1** and the results of the thermal rearrangement of the adducts.[9]

Results and Discussion

The results of the cycloadditions of nitrones **2a–f** to **1** are shown in Table 1. The cycloadditions to **1**, despite its being a tetrasubstituted alkene,[10] were carried out under relatively mild conditions (rt or 60 °C) using long reaction times (from 7 to 30 days). Prolonged reaction times instead of increased reaction temperatures proved to be necessary because of the low thermal stability of the cycloadducts (see below). The unexpectedly high reactivity of **1** in nitrone cycloadditions has to be related to its peculiar electronic properties, particularly to its abnormally high lying HOMO.[7a] The yields of bisspirocyclopropaneisoxazolidines **3a–f** were good to moderate and depended on the reactivity and the stability of the nitrones involved.

The structural assignments were unequivocally made on the basis of their ^1H and ^{13}C NMR spectra. They show signals of the eight protons on the cyclopropane ring (δ 0–1 ppm), the four respective carbons (δ 4–11 ppm), and the proton bound to C3 on the isoxazolidine ring (singlet at δ 3.85 for **3a**, 3.48 for **3e**, and 4.83 for **3f**, multiplet with typical values of vicinal coupling constants at δ 3.57, 3.56, and 3.46 for **3b**, **3c**, and **3d**, respectively).

The thermal rearrangements of isoxazolidines **3a–f** (see Table 1) were achieved by heating 0.5–1 M solutions in appropriate aromatic solvents at reflux temperatures. As expected on the basis of the different thermal behavior observed for the 5- and 4-spirocyclopropaneisoxazolidines,[2,3] the two spirocyclopropane rings on C4 and C5 (isoxazolidine numbering) show different reactivity upon heating and only the cyclopropane ring in the 5-position, adjacent to the labile N–O bond, is involved in the thermal rearrangement. Thus, the totally chemoselective rearrangement afforded 3-spirocyclopropanepyridones **4a–f** in good yields.

The structural assignment was based on the observation of the characteristic signals for the piperidone carbonyl group (^{13}C NMR δ 208.7, 209.0, 210.1, 208.6, 206.1, and 208.3 for **4a–f**, respectively; IR 1686–1690 cm^{-1}) and for the cyclopropane moiety. The four protons on the cyclopropane ring are differentiated by the anisotropy of the carbonyl group, as two protons resonated at δ 0.4–0.8 and the other two at δ 1–1.4 (with the exception of **4e**, because of the influence of the vicinal ester group). The methyne protons α to the nitrogen gave singlets in the ^1H NMR spectrum of **4a** (δ 3.47), **4e** (δ 3.01), and **4f** (δ 4.24).

It is remarkable that, in every instance except entry 6, the thermal rearrangement selectively provided cyclic

(9) Preliminary communication: Brandi, A.; Goti, A.; Kozhushkov, S. I.; de Meijere, A. *J. Chem. Soc., Chem. Commun.* **1994**, 2185.

(10) Ordinary tetraalkyl-substituted alkenes do not cycloadd nitrones. Cf. Grünanger, P.; Vita-Finzi, P. *Isoxazoles–Part One. In The Chemistry of Heterocyclic Compounds*; Taylor, E. C., Weissberger, A., Series Eds.; John Wiley: New York, 1991.

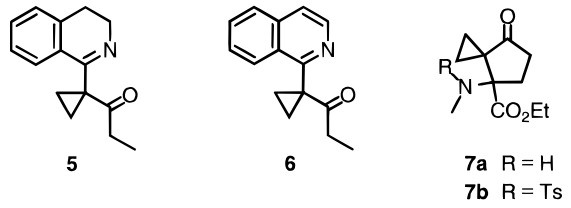
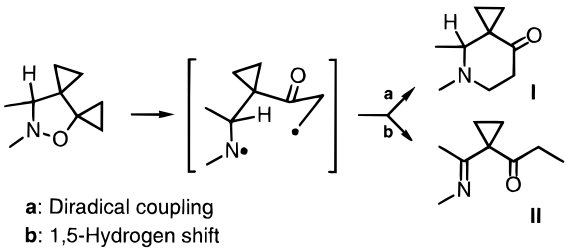


Figure 1.

Scheme 2

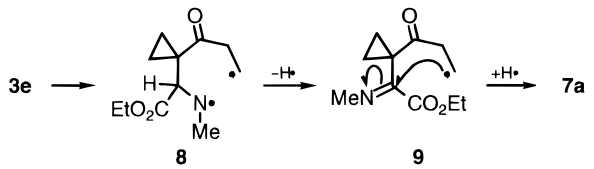


products, without the formation of open-chain isomers, which are usually obtained as side products from 5-spirocyclopropaneisoxazolidines.[2a,3] This result might be ascribed to the presence of the spiro-fused cyclopropane ring that raises the rotational barriers in the diradical intermediate increasing the proportion of reactive rotamers, thus favoring the diradical coupling[11] (path a in Scheme 2). A similar effect brought about by a cyclopropane ring, which increased the cyclization rate by a factor of 10, has recently been reported.[12]

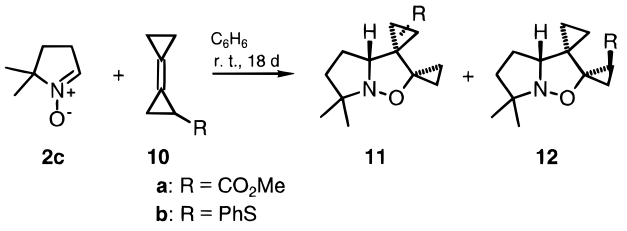
Only isoxazolidine **3f** gave an open-chain compound of type **II** (Scheme 2) in 24% yield besides cyclic ketone **4f** (50%). In this case, the 1,5-hydrogen shift is probably facilitated by the mobility of the benzylic proton and by the possible formation of a stable conjugated imine (**5**). As a matter of fact, when the sample is heated for a longer time, the aromatized isoquinoline derivative **6** can also be obtained in low yield (8%) (Figure 1).

An isomeric side product was also observed in the rearrangement of isoxazolidine **3e**, in a ratio 1:4 along with ketone **4e**. It was difficult to separate this compound from the major isomer; therefore its spectroscopic data could only be obtained from those of enriched fractions. The new compound did not show any analogy with compounds of type **II**, and it was tentatively assigned the structure **7a** on the basis of its spectral data. The ^{13}C NMR spectrum of **7a** showed diagnostic signals for a cyclopentanone bearing a secondary amino substituent, i.e., a deshielded carbonyl group (δ 215.7 vs 206.1 for **4e**), a quaternary carbon (δ 68.6), and a nitrogen-bound methyl group resonating 13 ppm upfield with respect to the same methyl in **4e** (δ 30.7 vs 43.7). In the ^1H NMR spectrum no signal for an isolated C−H was found, and the signals of the methylene groups, relatively shielded, are not in accordance with protons adjacent to nitrogen. Final confirmation of the structure was proven by the direct derivatization of **7a** to the corresponding tosylate **7b** in the crude reaction mixture. Compound **7b** was easily separable from **4e**, and complete characterization, including elemental analysis, was carried out. The formation of cyclic isomer **7a** can be rationalized with the loss of a hydrogen adjacent to the nitrogen in diradical intermediate **8** to afford imine

Scheme 3



Scheme 4



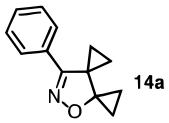
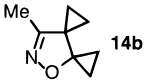
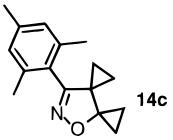
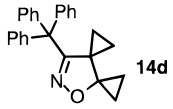
radical **9** which then undergoes a facile *5-exo-trig* cyclization (Scheme 3).

An attempt to purify **3c** by distillation under reduced pressure (10^{-2} Torr), at too low a temperature to give the rearrangement (40 °C), led to the partial decomposition to nitrone **2c** by a retrocycloaddition process. Retrocycloadditions are well-known in the literature,[13] particularly in the case of adducts derived from five-membered cyclic nitrones. In the case of isoxazolidines of type **3**, the retrocycloaddition might also be favored by the strain of the 2-fold spirocyclopropane annelation. In order to avoid these retrocycloadditions and to simultaneously increase the yield of the final ketone, the two-step procedure was turned into a more convenient "one-pot" process. Toward that end, the mixture of the starting materials was heated directly for the appropriate time at the temperature required for the rearrangement to occur. The results are shown in the last column of Table 1. As expected, the yields in comparision with those calculated for the two-step procedure, which are reported in parentheses, were significantly improved in every case. Only with nitrone **2b** did the "one-pot" process fail, probably due to the instability of the nitrone upon prolonged heating at high temperature.

As the cycloaddition rearrangement process[2,3] applied to BCP (**1**) has proved to be of high efficiency in the synthesis of new interesting heterocyclic α-spirocyclopropane annelated ketones, some of which have proved to be DNA cleaving agents with promising potential,[14] it might favorably be extended by the use of substituted bicyclopropylidenes, in order to obtain selectively substituted heterocycles. To test for this possibility, cycloadditions of the nitrone **2c** to monosubstituted bicyclopropylidenes **10a** and **10b**[15] were carried out (Scheme 4). Unfortunately, in both cases complex mixtures of four isomeric isoxazolidines **11** and **12** with very little selectivity, albeit in high yield, were obtained. The mixtures could neither be separated by chromatography nor simplified by thermal rearrangement, no matter whether reactions were carried out in two steps or in one pot. These results indicate that only unsubstituted or, possibly, symmetrically disubstituted BCPs can be synthetically useful in this domino process.

(11) Bruice, T. C.; Pandit, U. K. *J. Am. Chem. Soc.* **1960**, *82*, 5858.
(12) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1991**, *113*, 224.
(13) Bianchi, G.; Gandolfi, R. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; John Wiley: New York, 1984; Vol. 2, p 451.
(14) Goti, A.; Anichini, B.; Brandi, A.; de Meijere, A.; Citti, L.; Nevischi, S. *Tetrahedron Lett.* **1995**, *36*, 5811.
(15) de Meijere, A.; Kozhushkov, S. I.; Zefirov, N. S. *Synthesis* **1993**, 681.

Table 2. Cycloadditions of Nitrile Oxides 13a–d to BCP

Entry	Nitrile oxide	Reaction Conditions	Cycloadduct	Yield (%)
1	Ph–CNO **13a**	THF, 66 °C, 7 h	 **14a**	40
2	Me-CNO **13b**	Et_2O, 20 °C, 7 d	 **14b**	<10
3	2,4,6-$Me_3C_6H_2$-CNO **13c**	C_6H_5Me, 110 °C, 48 h	 **14c**	67
4	Ph_3C-CNO **13d**	C_6H_5Me, 110 °C, 7 d	 **14d**	17

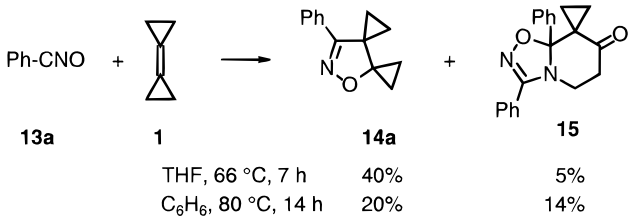
Nitrile oxides are more reactive than nitrones in 1,3-dipolar cycloadditions toward unactivated alkenes, because of their low-lying LUMO. On the other hand, they are also much less stable, mainly due to their facile dimerization to furoxans. The dimerization of nitrile oxides is largely preferred, when rather unreactive dipolarophiles such as bicyclopropylidene (**1**) are present. In such cases, however, stable nitrile oxides with bulky substituents adjacent to the CNO group that hamper dimerization can be used, but they usually need much higher reaction temperatures before the cycloaddition will occur. To study nitrile oxide cycloadditions onto **1**, two reactive nitrile oxides (**13a,b**) and two sterically congested nitrile oxides (**13c,d**) were used (see Table 2).

The cycloaddition of benzonitrile oxide (**13a**) at room temperature gave a poor yield of the adduct **14a** (less than 10%), together with extensive formation of 3,4-diphenylfuroxan. A somewhat better yield (40%, entry 1, Table 2) was obtained when **13a** was slowly generated by adding the corresponding benzohydroximoyl chloride to a refluxing solution of **1** in THF in presence of $NaHCO_3$. The more reactive acetonitrile oxide (**13b**), generated *in situ* from nitroethane according to Mukaiyama's method,[16] gave, either at room temperature or in refluxing ethereal solvents, very poor yields of **14b**, which could not be completely separated by flash chromatography from the mass of undesired dimethylfuroxan. Mesitonitrile oxide (**13c**) needs much higher temperatures to react, but in refluxing toluene gave a reasonably high yield (67%) of isoxazoline **14c** (entry 3, Table 2). Under the same conditions, triphenylacetonitrile oxide (**13d**) (entry 4, Table 2) is too sluggish to react at an acceptable rate.

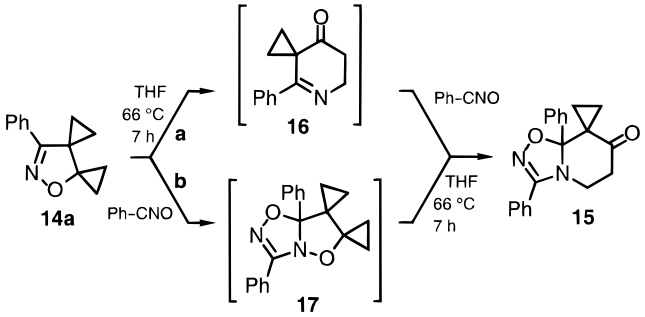
The structural assignment to adducts **14a–d** rests on the observation of eight cyclopropane protons in the ^1H NMR spectrum (multiplets at δ 0.4–1.2 for **14a–c** and at δ −0.10–1.13 for **14d**) and of the corresponding carbons (which give two signals for each compound at δ 7–10) and of the C=N group (δ 162–165) in the ^{13}C NMR spectrum.

Despite the poor results in most cases, except **14c**, the formation of cycloadducts is relevant, considering the tetrasubstitution of the double bond in BCP (**1**).[10] In the reaction of **13a** with **1**, a solid product was isolated in small quantity (5%) in addition to isoxazoline **14a**. Its formation depended on the reaction conditions, increasing at higher temperatures and longer times. The structure **15** was assigned to the product (Scheme 5) on the basis of the similarity of its NMR spectra with those of rearrangement products **4** from the corresponding isoxazolidines **3**. Indeed, the ^{13}C NMR spectrum showed the carbonyl group (δ 206.7) and two methylene carbons of the cyclopropane ring (δ 14.9 and 13.6). On the other hand, the ^1H NMR spectrum showed the methylenic protons of the piperidone ring differentiated (δ 3.74, 3.51, 2.91 and 2.61) and four cyclopropyl protons at δ 1.45–0.38.

Scheme 5



Scheme 6

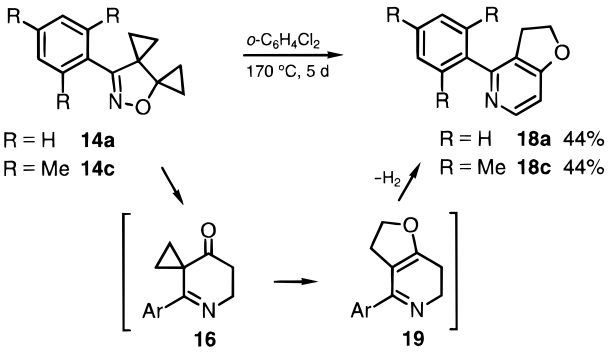


Compound **15** was derived, according to elemental analysis and mass spectral data, from the reaction of two molecules of benzonitrile oxide (**13a**) and one molecule of BCP (**1**). Its formation may be accounted for along two alternative routes (Scheme 6). Either primary monoadduct **14a** first rearranges to **16** at the reaction temperature (66 °C), and **16** subsequently cycloadds a second molecule of **13a** (route **a** in Scheme 6), or the second molecule of **13a** first cycloadds to isoxazoline **14a** to give isoxazolidine **17**, which then undergoes a thermal rearrangement to **15** (route **b**).

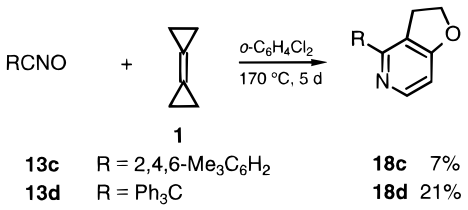
Normally, spirocyclopropane-annelated isoxazolines require for rearrangement higher temperatures than the corresponding isoxazolidines, and also a higher temperature than that involved in the reaction (66 °C). Indeed, route **a** was ruled out after the demonstration that prolonged heating of **14a** in refluxing THF, under the same conditions as applied for the cycloaddition, led to quantitative recovery of the starting material. On the contrary, the second hypothesis (route **b**) was confirmed by generating **13a** in a refluxing THF solution of pure **14a**, which provided **15** as the only product, besides the starting material and 3,4-diphenylfuroxan. Few examples of formation of side products by nitrile oxide cycloaddition to the C=N double bond of isoxazolines at room temperature have been reported in the literature, just limited to benzonitrile oxide or its derivatives.[17] In one single example the bis-adduct was the major product when the cycloaddition was carried out at higher tem-

(16) Mukaiyama, T.; Hoshino, T. *J. Am. Chem. Soc.* **1960**, *82*, 5339.

Scheme 7



Scheme 8



perature.[18] In our case, the amount of side product **15** was sensibly increased by running the reaction in refluxing benzene (14% vs 5%, Scheme 5).

As shown, 5-spirocyclopropaneisoxazolines undergo the thermal rearrangement at higher temperatures than the isoxazolidine counterparts.[2] In fact, **14a** and **14c** were stable below 140 °C in solution. At 170 °C in *o*-dichlorobenzene, however, they both cleanly rearranged to afford dihydrofuro[2,3-*c*]pyridines **18a** and **18c** (Scheme 7).

In the ^{1}H NMR spectra of **18** no signal of cyclopropane protons could be observed, but signals for the dihydrofuran ring (δ 4.65 and 4.63 for the methylene protons α to the oxygen and δ 3.43 and 2.90 for the ones in β for **18a** and **18c**, respectively) and for the pyridine ring (δ 8.41 and 6.73 for **18a** and δ 8.39 and 6.73 for **18c**) were detectable. This confirmed a complete aromatization of the pyridine ring.

The mechanistic rationale for the formation of products **18** rests on the usual initial rearrangement of cycloadducts **14** to tetrahydropyridones **16**. These compounds are probably very unstable under the harsh reaction conditions used and undergo also the second cyclopropane ring fission *via* a thermal acylcyclopropane−dihydrofuran rearrangement to tetrahydrofuropyridines **19**. Eventually aromatization of the dihydropyridine ring may easily occur under the reaction conditions to give final products **18** (Scheme 7). This acylcyclopropane−tetrahydrofuran rearrangement closely resembles the vinylcyclopropane−cyclopentene rearrangement, but does not readily occur under simple thermal activation.[19] Finally, with stable nitrile oxide **13d** the cycloaddition and the rearrangement can be achieved in one single operation at high temperature to afford dihydrofuropyridine **18d** in higher overall yield (Scheme 8). However, dihydrofuropyridine **18c** was obtained in poor yield (7%) in the corresponding one-pot reaction of **1** with nitrile oxide **13c** because of its rearrangement to the corresponding isocyanate at 170 °C.

In conclusion, we have established a convenient access to functionalized azaheterocycles by the extension of the nitrone (or nitrile oxide) cycloaddition−rearrangement methodology[2] to readily available bicyclopropylidene **1**.[8] Studies are underway in our laboratories in order to outline useful synthetic elaborations of the rearranged spirocyclopropane heterocycles, one example of which has already been reported here in the ring expansion to dihydrofuropyridines.

Experimental Section

All the reactions were carried out under nitrogen or in sealed tubes, and the solvents were appropriately dried before use. R_f values refer to TLC on 0.25 mm silica gel plates (Merck F_{254}) obtained using the same eluent as in the column chromatographies. Melting points were determined on a 510 Büchi apparatus. NMR spectra were recorded on a Varian Gemini (^{1}H, 200 MHz), with $CDCl_3$ as solvent; the NMR data are reported in δ (ppm) from TMS. IR spectra were recorded in $CDCl_3$ solution on a Perkin-Elmer 881 spectrophotometer. Mass spectra were recorded at 70 eV by GC inlet on a 5790A-5970A Hewlett-Packard instrument or by direct inlet (for the thermally labile cycloadducts) on a QMD 1000 Carlo Erba instrument. Elemental analyses were performed with a Perkin-Elmer 240 C analyzer. BCP derivatives used in this work were prepared according to published procedures.[8,15]

Cycloaddition of Nitrone 2a to Bicyclopropylidene (1). A solution of **1** (160 mg, 2 mmol) and **2a** (203 mg, 1.5 mmol) in benzene (0.5 mL) was heated in a sealed tube at 60 °C for 30 d. After cooling to room temperature, the solvent was removed *in vacuo* and the crude product was purified by flash chromatography on silica gel (eluent CH_2Cl_2−CH_3OH 30:1) to give the cycloadduct **3a** (R_f 0.44, 300 mg, 1.4 mmol, 93%) as an oil.

8-Methyl-9-phenyl-7-oxa-8-azadispiro[2.0.2.3]nonane (3a): ^{1}H NMR δ 7.33 (m, 5H), 3.85 (s, 1H), 2.77 (s, 3H), 0.97 (m, 2H), 0.65−0.30 (m, 4H), 0.20−0.03 (m, 2H); ^{13}C NMR δ 137.8 (s), 128.8 (d, 2C), 128.3 (d, 2C), 127.9 (d), 79.7 (d), 66.7 (s), 44.7 (q), 33.6 (s), 9.9 (t), 8.4 (t), 6.9 (t), 6.5 (t); IR 3084, 3031, 3003, 2961, 1602, 1491, 1452, 1434 cm^{-1}; MS *m*/*z* 215 (M^+, 8), 214 (4), 186 (14), 158 (69), 146 (31), 130 (36), 129 (100), 128 (39), 120 (31), 118 (96), 115 (80), 91 (42), 77 (54). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 77.91; H, 8.01; N, 6.32.

Cycloaddition of Nitrone 2b to Bicyclopropylidene (1). A solution of **1** (110 mg, 1.4 mmol) and **2b** (175 mg, 2.1 mmol) in benzene (2 mL) was stirred at room temperature for 20 d. The solvent was removed *in vacuo*, and the crude product was purified by flash chromatography on silica gel (eluent ethyl acetate) to give the cycloadduct **3b** (R_f 0.25, 96 mg, 0.58 mmol, 42%) as an oil.

Dispiro[cyclopropane-1,2′-hexahydropyrrolo[1,2-*b*]isoxazole-3,1″-cyclopropane] (3b): ^{1}H NMR δ 3.57 (t, J = 6.0 Hz, 1H), 3.37−3.26 (m, 1H), 3.25−3.05 (m, 1H), 2.01−1.85 (m, 1H), 1.81−1.58 (m, 3H), 0.89−0.37 (m, 6H), 0.19−0.08 (m, 2H); ^{13}C NMR δ 71.8 (d), 66.0 (s), 57.8 (t), 31.9 (s), 29.6 (t), 24.3 (t), 10.8 (t), 10.0 (t), 5.0 (t), 4.4 (t); IR 3079, 3004, 2971, 2875, 1444 cm^{-1}; MS *m*/*z* 165 (M^+, 8), 164 (16), 150 (6), 136 (35), 109 (28), 108 (81), 81 (45), 80 (100), 79 (72), 68 (49), 67 (56). Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.80; H, 9.04; N, 8.04.

Cycloaddition of Nitrone 2c to Bicyclopropylidene (1). A solution of **1** (264 mg, 3.3 mmol) and **2c** (373 mg, 3.3 mmol) in benzene (0.8 mL) was stirred at room temperature for 7 d. The solvent was removed *in vacuo*, and the crude product was

(17) (a) Bettinetti, G. F.; Gamba, A. *Gazz. Chim. Ital.* **1970**, *100*, 1144. (b) Caramella, P.; Frattini, P.; Grünanger, P. *Tetrahedron Lett.* **1971**, 3817. (c) Bianchi, G.; De Micheli, C.; Gandolfi, R. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1711. (d) Gibert, J.-P.; Jacquier, R.; Pétrus, C. *Bull. Soc. Chim. Fr.* **1979**, 281. (e) Adembri, G.; Donati, D.; Fusi, S.; Ponticelli, F. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2033. (f) Gandolfi, R.; Tonoletti, G.; Rastelli, A.; Bagatti, M. *J. Org. Chem.* **1993**, *58*, 6038.

(18) Stverkova, S.; Zak, Z.; Jonas, J. *Liebigs Ann. Chem.* **1993**, 1169.

(19) (a) Hudlicky, T.; Reed, J. W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1990; Vol. 8, p 941 and references cited therein. (b) Hofmann, B.; Reissig, H.-U. *Chem. Ber.* **1994**, *127*, 2327. (c) Lund, E. A.; Kennedy, I. A.; Fallis, A. G. *Tetrahedron Lett.* **1993**, *34*, 6841. (d) Lee, P. H.; Kim, J. S.; Kim, Y. C.; Kim, S. *Tetrahedron Lett.* **1993**, *34*, 7583.

purified by flash chromatography on silica gel (eluent CH_2Cl_2−CH_3OH 24:1) to give the cycloadduct **3c** (R_f 0.26, 509 mg, 2.6 mmol, 80%).

Dispiro[cyclopropane-1,2′-6,6-dimethylhexahydropyrrolo[1,2-*b*]isoxazole-3,1″-cyclopropane] (3c): colorless liquid, bp 40 °C/0.1 Torr; ^{1}H NMR δ 3.56 (dd, J = 8.8, 4.3 Hz, 1H), 2.15−1.80 (m, 3H), 1.60 (m, 1H), 1.29 (s, 3H), 1.04 (s, 3H), 0.82−0.53 (m, 5H), 0.50−0.40 (m, 1H), 0.22−0.05 (m, 2H); ^{13}C NMR δ 72.3 (d), 69.0 (s), 65.8 (s), 36.3 (t), 33.0 (s), 30.1 (t), 26.6 (q), 24.1 (q), 11.8 (t), 9.9 (t), 5.1 (t), 4.3 (t); IR 3079, 2999, 2972, 2943, 2871, 1450, 1365 cm^{-1}; MS m/z 193 (M$^+$, 7), 192 (11), 178 (84), 136 (31), 122 (66), 108 (37), 96 (100), 94 (82), 82 (54), 81 (61), 79 (43). Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.63; H, 10.09; N, 7.69.

Cycloaddition of Nitrone 2d to Bicyclopropylidene (1). A solution of **1** (215 mg, 2.7 mmol) and **2d** (392 mg, 4.0 mmol) in benzene (3 mL) was heated in a sealed tube at 60 °C for 7 d. After cooling to room temperature, the solvent was removed *in vacuo* and the crude product was purified by flash chromatography on silica gel (eluent CH_2Cl_2−CH_3OH 30:1) to give the cycloadduct **3d** (R_f 0.34, 180 mg, 1.0 mmol, 37%) as an oil.

Dispiro[cyclopropane-1,2′-hexahydro[2*H*]isoxazolo-[2,3-*a*]pyridine-3,1″-cyclopropane] (3d): ^{1}H NMR: δ 3.46 (m, 1H), 2.71 (br d, J = 10.0 Hz, 1H), 2.54 (dt, J = 5.0, 9.5 Hz, 1H), 1.76 (m, 3H), 1.50−1.15 (m, 3H), 0.85 (m, 2H), 0.70 (dt, J = 9.4, 4.6 Hz, 1H), 0.50−0.10 (m, 5H); ^{13}C NMR δ 71.74 (d), 66.2 (s), 55.8 (t), 28.8 (s), 26.01 (t), 24.8 (t), 23.2 (t), 9.6 (t), 7.0 (t), 5.8 (t), 4.5 (t); IR 3080, 3007, 2948, 2859, 1443 cm^{-1}; MS m/z 179 (M$^+$, 15), 178 (6), 150 (33), 136 (28), 122 (64), 108 (39), 100 (94), 94 (50), 55 (65), 41 (100). Anal. Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.81. Found: C, 73.91; H, 9.41; N, 7.84.

Cycloaddition of Nitrone 2e to Bicyclopropylidene (1). A solution of **1** (200 mg, 2.5 mmol) and **2e** (327 mg, 2.5 mmol) in THF (2 mL) was stirred at room temperature for 16 d. The solvent was removed *in vacuo*, and the crude product was purified by flash chromatography on silica gel (eluent petroleum ether−diethyl ether 1:4) to give the cycloadduct **3e** (R_f 0.39, 418 mg, 1.98 mmol, 79%) as an oil.

8-Methyl-9-(ethoxycarbonyl)-7-oxa-8-azadispiro[2.0.2.3]-nonane (3e): ^{1}H NMR δ 4.20 (m, 2H), 3.48 (s, 1H), 2.87 (s, 3H), 1.26 (t, J = 7.3 Hz, 3H), 0.89−0.60 (m, 5H), 0.45−0.16 (m, 3H); ^{13}C NMR δ 169.8 (s), 75.6 (d), 66.1 (s), 61.0 (t), 46.2 (q), 30.3 (s), 14.2 (q), 10.4 (t), 9.1 (t), 6.1 (t), 5.2 (t); IR 3085, 2986, 2878, 1741, 1445, 1274 cm^{-1}; MS m/z 211 (M$^+$, 5), 154 (4), 138 (25), 110 (80), 69 (100). Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.11; N, 6.63. Found: C, 62.47; H, 8.50; N, 6.58.

Cycloaddition of Nitrone 2f to Bicyclopropylidene (1). A solution of **1** (200 mg, 2.5 mmol) and **2f** (451 mg, 3.1 mmol) in benzene (2.5 mL) was stirred at room temperature for 10 d. The solvent was removed *in vacuo*, and the crude product was purified by flash chromatography on silica gel (eluent petroleum ether−diethyl ether 1:4) to give the cycloadduct **3f** (R_f 0.51, 415 mg, 1.8 mmol, 73%) as a solid.

Dispiro[cyclopropane-1,1′-1,5,6,10b-tetrahydro(2*H*)-isoxazolo[3,2-*a*]isoquinoline-2,1″-cyclopropane] (3f): mp 55−56.5 °C; ^{1}H NMR δ 7.19−7.02 (m, 3H), 6.84−6.78 (m, 1H), 4.83 (s, 1H), 3.60 (dt, J = 4.3, 10.7 Hz, 1H), 3.25 (dt, J = 10.3, 4.2 Hz, 1H), 3.06 (ddd, J = 16.1, 11.0, 4.7 Hz, 1H), 2.85 (dt, J = 16.1, 3.7 Hz, 1H), 0.88 (m, 2H), 0.67−0.53 (m, 1H), 0.48−0.38 (m, 1H), 0.32−0.11 (m, 3H), 0.07−(−0.02) (m, 1H); ^{13}C NMR δ 134.4 (s), 132.5 (s), 128.3 (d), 127.1 (d), 125.9 (d, 2C), 67.1 (s), 66.9 (d), 49.8 (t), 30.3 (s), 28.7 (t), 8.2 (t), 8.1 (t), 7.8 (t), 3.2 (t); IR 3077, 3027, 3005, 2968, 2872, 1601, 1489, 1452, 1427 cm^{-1}; MS m/z 227 (M$^+$, 12), 226 (12), 198 (88), 170 (72), 131 (42), 130 (100), 128 (52), 86 (40), 84 (62). Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.52; H, 7.60; N, 5.84.

General Procedure for the Thermal Rearrangement of Adducts 3a−d. A solution of 1 mmol of **3a−d** in 1 mL of the appropriate solvent was heated in a sealed tube at the temperature and time indicated in Table 1. After cooling to room temperature, the solvent was removed *in vacuo* and the crude mixture was chromatographed on silica gel to give the rearranged piperidones **4a−d**.

5-Methyl-4-phenyl-5-azaspiro[2.5]octan-8-one (4a): oil, R_f 0.29 (CH_2Cl_2−CH_3OH 19:1), 63% yield; ^{1}H NMR δ 7.35−7.22 (m, 3H), 7.20−7.10 (m, 2H), 3.47 (s, 1H), 3.06 (m, 1H), 2.85−2.70 (m, 1H), 2.70−2.60 (m, 2H), 2.28 (s, 3H), 1.26 (m, 2H), 0.80−0.65 (m, 1H), 0.55−0.40 (m, 1H); ^{13}C NMR δ 208.7 (s), 137.8 (s), 129.4 (d, 2C), 128.0 (d, 2C), 127.6 (d), 72.5 (d), 50.0 (t), 44.2 (q), 38.8 (t), 32.0 (s), 18.4 (t), 14.8 (t); IR: 3087, 3065, 3031, 3005, 2958, 2850, 1686, 1446, 1364 cm^{-1}; MS m/z 215 (M$^+$, 15), 214 (3), 146 (12), 138 (100), 118 (33), 77 (19). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 77.90; H, 8.02; N, 6.35.

Spiro[cyclopropane-1,8′-octahydroindolizin-7-one] (4b): oil, R_f 0.41 ($CHCl_3$−CH_3OH + 1% NH_4OH 10:1), 60% yield; ^{1}H NMR δ 3.34−3.24 (m, 1H), 3.23−3.10 (m, 1H), 2.77−2.40 (m, 4H), 2.27 (q, J = 8.9 Hz, 1H), 2.01−1.69 (m, 2H), 1.64−1.45 (m, 2H), 1.40−1.10 (m, 2H), 0.78−0.64 (m, 1H), 0.55−0.44 (m, 1H); ^{13}C NMR δ 209.0 (s), 65.4 (d), 54.6 (t), 50.0 (t), 38.9 (t), 32.2 (s), 25.8 (t), 22.0 (t), 15.2 (t), 10.6 (t); IR 3009, 2960, 2808, 2756, 1689, 1459, 1346 cm^{-1}; MS m/z 165 (M$^+$, 16), 164 (100), 136 (22), 122 (21), 108 (22), 96 (100). Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.58; H, 9.42; N, 8.09.

Spiro[cyclopropane-1,8′-3,3-dimethyloctahydroindolizin-7-one] (4c): oil, R_f 0.23 (CH_2Cl_2−CH_3OH 24:1), 76% yield; ^{1}H NMR δ 3.23 (t, J = 7.8 Hz, 1H), 3.07 (m, 1H), 2.72−2.60 (m, 1H), 2.60−2.38 (m, 2H), 1.81−1.59 (m, 2H), 1.59−1.40 (m, 2H), 1.35−1.05 (m, 2H), 1.19 (s, 3H), 0.95 (s, 3H), 0.73 (ddd, J = 9.6, 7.2, 4.0 Hz, 1H), 0.46 (ddd, J = 9.2, 7.2, 3.8 Hz, 1H); ^{13}C NMR δ 210.1 (s), 62.0 (d), 60.3 (s), 42.3 (t), 40.0 (t), 38.5 (t), 33.0 (s), 27.6 (q), 23.0 (t), 19.5 (q), 16.0 (t), 10.5 (t); IR 3095, 3008, 2967, 2871, 2813, 2759, 2701, 1686, 1556, 1456, 1381 cm^{-1}; MS m/z 193 (M$^+$, 4), 192 (5), 178 (100), 94 (20). Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.18; H, 9.97; N, 7.56.

Spiro[cyclopropane-1,1′-octahydroquinolizin-2-one] (4d): oil, R_f 0.16 (CH_2Cl_2−CH_3OH 20:1), 68% yield; ^{1}H NMR δ 3.15−2.98 (m, 2H), 2.85−2.35 (m, 4H), 2.15 (m, 1H), 1.85−1.45 (m, 4H), 1.35−1.05 (m, 4H), 0.68 (m, 2H); ^{13}C NMR δ 208.6 (s), 63.0 (d), 57.0 (t), 53.7 (t), 39.4 (t), 32.0 (s), 27.0 (t), 25.0 (t), 23.6 (t), 16.5 (t), 11.0 (t); IR 3019, 2946, 2862, 2814, 2771, 1690, 1657, 1350 cm^{-1}; MS m/z 179 (M$^+$, 22), 178 (100), 150 (54), 122 (37), 110 (69). Anal. Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.81. Found: C, 73.59; H, 9.53; N, 7.57.

Thermal Rearrangement of the Adduct 3e. A solution of **3e** (146 mg, 0.69 mmol) in 1.5 mL of toluene was heated in a sealed tube at 110 °C for 4 d. After cooling to room temperature, the solution was concentrated *in vacuo* and the crude product was chromatographed on a column of silica gel (eluent CH_2Cl_2−CH_3OH + 1% NH_4OH 50:1) to give a mixture of **4e** and **7a** (112 mg, 0.53 mmol, 76%) in a 4:1 ratio. Further chromatographic separation with the same eluent gave **4e** as an analytically pure oil, and mixtures of **4e** and **7a**, enriched in the latter component.

4-(Ethoxycarbonyl)-5-methyl-5-azaspiro[2.5]octan-8-one (4e): oil, R_f 0.13; ^{1}H NMR δ 4.18 (q, J = 7.1 Hz, 2H), 3.24 (ddd, J = 12.1, 9.9, 5.5 Hz, 1H), 3.04−2.92 (m, 1H), 3.01 (s, 1H), 2.74−2.43 (m, 2H), 2.51 (s, 3H), 1.67−1.56 (m, 1H), 1.26 (t, J = 7.1 Hz, 3H), 1.06−0.93 (m, 2H), 0.65−0.55 (m, 1H); ^{13}C NMR δ 206.1 (s), 170.1 (s), 70.9 (d), 60.6 (t), 48.7 (t), 43.7 (q), 38.1 (t), 29.5 (s), 21.3 (t), 14.4 (q), 10.1 (t); IR 2983, 2942, 2858, 1725 (covers the piperidone C=O absorbance), 1445, 1366 cm^{-1}; MS m/z 139 (26), 138 (M$^+$ − COOEt, 100), 120 (29), 96 (28). Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.11; N, 6.63. Found: C, 62.27; H, 7.80; N, 7.00.

7-(Ethoxycarbonyl)-7-(methylamino)spiro[2.4]heptan-4-one (7a): R_f 0.11; ^{1}H NMR δ 4.15 (q, J = 7.1 Hz, 2H), 2.70−2.20 (m, 5H), 2.28 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H), 1.20−1.00 (m, 3H), 0.80−0.70 (m, 1H); ^{13}C NMR δ 215.7 (s), 173.0 (s), 68.6 (s), 61.0 (t), 38.6 (s), 35.4 (t), 30.7 (q), 26.0 (t), 16.6 (t), 14.3 (q), 11.5 (t); MS m/z 138 (M$^+$ − COOEt, 100), 81 (3), 68 (3), 42 (4).

In another run, 545 mg of a crude mixture of **4e** and **7a** (4:1 ratio) obtained from **1** and **2e** (3 mmol each) was directly treated with *p*-toluenesulfonyl chloride (190 mg, 1 mmol) in pyridine (5 mL) and stirred at rt for 15 h. After concentration in vacuo, the residue was washed with saturated Na_2CO_3,

extracted with Et_2O (3 × 6 mL), and dried over Na_2SO_4. The crude product was chromatographed on a column of silica gel (eluent diethyl ether) to give **7b** (117 mg, 0.32 mmol, 11% based on **1**) and **4e** (220 mg, 1.04 mmol, 35% based on **1**).

7-(Ethoxycarbonyl)-7-((4-methylbenzenesulfonyl)-methylamino)spiro[2.4]heptan-4-one (7b): oil, R_f 0.60; ^{1}H NMR δ 7.79 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 4.24 (dq, J = 2.0, 7.1 Hz, 2H), 2.98−2.90 (m, 2H), 2.81 (s, 3H), 2.48−2.30 (m, 2H), 2.40 (s, 3H), 1.64−1.56 (m, 1H), 1.31 (t, J = 7.1 Hz, 3H), 1.33−0.85 (m, 3H); ^{13}C NMR δ 214.0 (s), 170.6 (s), 143.8 (s), 136.7 (s), 129.6 (d, 2C), 127.6 (d, 2C), 72.8 (s), 62.0 (t), 36.8 (s), 35.3 (t), 33.3 (q), 31.7 (s), 21.5 (q), 20.9 (t), 14.3 (t), 14.1 (q); MS m/z 294 (6), 292 (M^+ − COOEt, 100), 155 (30), 137 (15), 91 (43). Anal. Calcd for $C_{18}H_{23}NO_5S$: C, 59.16; H, 6.34; N, 3.83. Found: C, 59.43; H, 6.46; N, 3.47.

Thermal Rearrangement of the Adduct 3f. A solution of **3f** (198 mg, 0.87 mmol) in 1.5 mL of xylenes was heated in a sealed tube at 125 °C for 5 d. After cooling to room temperature, the solvent was removed *in vacuo* and the crude product was chromatographed on a column of silica gel (eluent ethyl acetate) to give **4f** (100 mg, 0.44 mmol, 50%) and a 3:1 mixture of **5** and **6** (64 mg, 32%). Spectral and analytical data for **5** and **6** refer to highly enriched fractions in each compound obtained after repeated purification.

Spiro[cyclopropane-1,1′-2-oxo-1,2,3,4,5,6,7,11b-octahydropyrido[2,1-*a*]isoquinoline] (4f): oil, R_f 0.16; ^{1}H NMR δ 7.16−6.96 (m, 4H), 4.24 (s, 1H), 3.54−3.25 (m, 3H), 3.06−2.93 (m, 3H), 2.73−2.40 (m, 2H), 1.41−1.30 (m, 1H), 1.04−0.94 (m, 1H), 0.79−0.70 (m, 1H), 0.49−0.39 (m, 1H); ^{13}C NMR δ 208.3 (s), 134.8 (s), 133.2 (s), 129.0 (d), 127.4 (d), 127.2 (d), 125.1 (d), 61.4 (d), 49.9 (t), 45.2 (t), 35.7 (t), 31.1 (s), 27.6 (t), 15.6 (t), 10.0 (t); IR 3080, 3025, 2927, 2852, 1689, 1597, 1542, 1438 cm^{-1}; MS m/z 227 (M^+, 33), 226 (57), 158 (100), 143 (27), 131 (38), 130 (55). Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.37; H, 7.44; N, 5.96.

1-(3,4-Dihydroisoquinolin-1-yl)-1-propionylcyclopropane (5): oil, R_f 0.52; ^{1}H NMR δ 7.75−7.18 (m, 4H), 3.71 (m, 2H), 2.74 (t, J = 7.4 Hz, 2H), 2.33 (q, J = 7.2 Hz, 2H), 1.56 (m, 2H), 1.31 (m, 2H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 209.3 (s), 165.3 (s), 137.6 (s), 130.9 (d), 128.9 (s), 127.7 (d), 127.1 (d), 125.4 (d), 47.3 (t), 34.0 (t), 29.6 (s), 25.6 (t), 17.1 (t, 2C), 7.9 (q); IR 3059, 2943, 2854, 1690, 1618, 1571, 1451 cm^{-1}; MS m/z 227 (M^+, 25), 226 (81), 212 (18), 198 (24), 170 (100), 156 (31). Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54, N, 6.16. Found: C, 78.77; H, 7.56, N, 5.85.

1-(Isoquinolin-1-yl)-1-propionylcyclopropane (6): oil, R_f 0.50; ^{1}H NMR δ 8.50 (d, J = 5.9 Hz, 1H), 8.13 (d, J = 8.5 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.72−7.64 (m, 3H), 2.16 (q, J = 7.2 Hz, 2H), 1.85 (m, 2H), 1.46 (m, 2H), 0.85 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 209.9 (s), 159.1 (s), 142.1 (d), 136.4 (s), 130.2 (d), 128.4 (s), 127.8 (d), 127.5 (d), 125.4 (d), 120.6 (d), 37.4 (s), 34.7 (t), 18.8 (t, 2C), 7.8 (q); IR 3120, 3058, 2981, 2875, 1691, 1619, 1561, 1498 cm^{-1}; MS m/z 225 (M^+, 38), 224 (65), 210 (82), 196 (54), 168 (91), 167 (100), 154 (54). Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.83; H, 6.78; N, 6.09.

One-Pot Reactions of Nitrones 2a,c−f with Bicyclopropylidene (1) To Yield 4a,c−f: General Procedure. A solution of BCP and the nitrone in the solvent appropriate for the rearrangement was heated in a sealed tube for the appropriate time. The reaction mixture was purified by flash chromatography on silica gel.

4a: 1 (204 mg, 2.5 mmol), **2a** (265 mg, 2.0 mmol), toluene (2 mL), 110 °C for 5 d, eluent CH_2Cl_2−CH_3OH 19:1, **4a** (257 mg, 61%).

4c: 1 (460 mg, 5.7 mmol), **2c** (390 mg, 3.5 mmol), benzene (2 mL), 80 °C for 7 d, eluent CH_2Cl_2−CH_3OH 24:1, **4c** (533 mg, 80%).

4d: 1 (144 mg, 1.8 mmol), **2d** (255 mg, 2.6 mmol), xylenes (2 mL), 125 °C for 6 d, eluent CH_2Cl_2−CH_3OH 20:1), **4d** (156 mg, 48%).

4e: 1 (168 mg, 2.1 mmol), **2e** (294 mg, 2.2 mmol), toluene (4 mL), 110 °C for 4 d, eluent CH_2Cl_2−CH_3OH + 1% NH_4OH 50:1, **4e** and **7a** (4:1, 296 mg, 67%).

4f: 1 (160 mg, 2 mmol), **2f** (382 mg, 2.6 mmol), xylenes (2.6 mL), 125 °C for 5 d, eluent CH_2Cl_2−CH_3OH + 1% NH_4OH 12:1, **4f** (R_f 0.13, 332 mg, 73%) and a fraction containing a 1:1.5 mixture of **5** and **6** (R_f 0.58, 35 mg, 8%).

Cycloaddition of Nitrone 2c to Methyl 1,1′-Bicyclopropylidene-2-carboxylate (10a). A solution of **10a** (317 mg, 2.3 mmol) and **2c** (339 mg, 3.0 mmol) in benzene (1.5 mL) was stirred at rt for 18 d. After concentration under reduced pressure, the residue was filtered through a short pad of silica gel (eluent ethyl acetate) to give a complex mixture of the four isomers **11a** and **12a** (533 mg, 2.1 mmol, 92%), in a 2.8:2.1:1.2:1 ratio.

11a and 12a: oil, R_f 0.51; ^{1}H NMR (values for the four methoxycarbonyl groups) δ 3.64 (s, 3H); 3.62 (s, 3H); 3.61 (s, 3H); 3.59 (s, 3H); ^{13}C NMR (values for the four C=O groups) δ 170.9 (s, 2C overlapped); 170.8 (s); 170.7 (s); (values for the four bridgehead carbons) δ 74.0 (d); 73.6 (d); 73.3 (d); 72.8 (d); IR 2971, 2875, 1726, 1437, 1366, 1226 cm^{-1}. Anal. Calcd for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42; N, 5.57. Found: C, 66.57; H, 8.47; N, 5.41.

Cycloaddition of Nitrone 2c to 2-(Phenylthio)-1,1′-bicyclopropylidene (10b). A solution of **10b** (94 mg, 0.5 mmol) and **2c** (57 mg, 0.5 mmol) in $CDCl_3$ (0.2 mL) was stirred at rt for 10 d. The ^{1}H NMR spectrum of the crude mixture showed that the four isomeric adducts **11b** and **12b** were formed in a 5.5:5:4:1 ratio.

11b and 12b: ^{1}H NMR (values for the bridgehead protons) δ 4.09−4.01 (m, 1H); 3.76−3.66 (m, 1H); 3.52 (m, 2H overlapped); ^{13}C NMR (values for the four bridgehead carbons) δ 73.6 (d); 73.3 (d); 73.1 (d); 72.8 (d).

Cycloaddition of Nitrile Oxide 13a to Bicyclopropylidene (1). A solution of benzohydroximoyl chloride[20] (513 mg, 3.3 mmol) in THF (10 mL) was added dropwise over 6 h to a stirred solution of **1** (240 mg, 3.0 mmol) containing $NaHCO_3$ (277 mg, 3.3 mmol) in THF (3 mL), and the solution was heated at reflux and stirred for an additional hour. The mixture was cooled to room temperature, and the salts were filtered off over Celite. Removal of the solvent *in vacuo* gave a crude mixture, which was purified by flash chromatography on silica gel (eluent petroleum ether−diethyl ether 4:1) to provide **14a** (240 mg, 1.2 mmol, 40%) and **15** (44 mg, 0.14 mmol, 5%). An analogous reaction carried out in refluxing benzene gave 20% of **14a** and 14% of **15**.

9-Phenyl-7-oxa-8-azadispiro[2.0.2.3]non-8-ene (14a): white solid, mp 87−89 °C (hexane), R_f 0.34; ^{1}H NMR δ 7.41 (m, 5H), 1.11 (m, 4H), 0.73 (m, 2H), 0.55 (m, 2H); ^{13}C NMR δ 161.8 (s), 129.7 (d, 2C), 128.6 (s and d, 2 C overlapped), 127.4 (d, 2C), 70.1 (s), 32.4 (s), 8.8 (t, 2C), 8.2 (t, 2C); IR 3089, 3064, 3009, 2962, 2947, 2926, 1459, 1444, 1367 cm^{-1}; MS m/z 199 (M^+, 40), 198 (100), 197 (26), 196 (65), 170 (53), 156 (39), 143 (42), 130 (33), 128 (37), 104 (46), 77 (61). Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.59; N, 7.03. Found: C, 78.73; H, 6.94; N, 6.63.

Spiro[cyclopropane-1,8′-3,8a-diphenyl-7-oxo-5,6,8,8a-tetrahydro-7*H*-1,2,4-oxadiazolo[4,5-*a*]pyridine (15): pale yellow solid, mp 84−86 °C, R_f 0.39; ^{1}H NMR δ 8.01−7.96 (m, 2H), 7.29−7.22 (m, 5H), 7.18−7.11 (m, 3H), 3.74 (ddd, J = 15.0, 11.8, 3.1 Hz, 1H), 3.51 (ddd, J = 15.0, 5.1, 3.6 Hz, 1H), 2.91 (ddd, J = 14.3, 11.8, 5.1 Hz, 1H), 2.61 (dt, J = 14.3, 3.3 Hz, 1H), 1.45−1.34 (dt, J = 4.4, 8.4 Hz, 1H), 0.96 (t, J = 8.4 Hz, 2H), 0.38 (ddd, J = 9.2, 7.7, 4.4 Hz, 1H); ^{13}C NMR δ 206.7 (s), 164.1 (s), 139.1 (s), 132.5 (d), 129.3 (d, 2C), 129.0 (d, 2C), 128.2 (d), 127.9 (d, 2C), 126.9 (d, 2C), 124.5 (s), 119.5 (s), 51.9 (t), 42.3 (t), 41.3 (s), 14.9 (t), 13.6 (t); IR 3068, 3031, 2945, 1765, 1680, 1640, 1514, 1443, 1336 cm^{-1}; MS m/z 318 (M^+, 5), 222 (12), 209 (6), 128 (27), 119 (23), 105 (100), 77 (44). Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.16; H, 5.75; N, 8.45.

Cycloaddition of Nitrile Oxide 13b to Bicyclopropylidene (1). Triethylamine (70 μL, 0.5 mmol) and **1** (380 mg, 4.75 mmol) were added to a stirred solution of nitroethane (356 mg, 4.75 mmol) and *p*-chlorophenyl isocyanate (1.69 g, 11 mmol) in diethyl ether (10 mL). The reaction mixture was stirred at rt for 7 d. Removal of the solvent *in vacuo* gave a crude mixture of the adduct **14b** and dimethylfuroxan in a 1:4

(20) Corsico Coda, A.; Tacconi, G. *Gazz. Chim. Ital.* **1984**, *114*, 131.

ratio. Compound **14b** could not be completely separated from dimethylfuroxan by flash chromatography on silica gel (eluent CH_2Cl_2).

9-Methyl-7-oxa-8-azadispiro[2.0.2.3]non-8-ene (14b): R_f 0.41; ^{1}H NMR δ 1.76 (s, 3H), 0.98 (m, 4H), 0.63 (m, 2H), 0.43 (m, 2H); ^{13}C NMR δ 160.2 (s), 67.9 (s), 31.8 (s), 9.3 (q), 8.3 (t, 2C), 7.9 (t, 2C); MS *m*/*z* 137 (M^+, 8), 122 (9), 81 (12), 68 (30), 40 (100), 39 (56).

Cycloaddition of Nitrile Oxide 13c to Bicyclopropylidene (1). A refluxing solution of **1** (103 mg, 1.3 mmol) and **13c**[21] (345 mg, 2.1 mmol) in toluene (3 mL) was stirred for 48 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo* and the crude product was purified by flash chromatography on silica gel (eluent petroleum ether−diethyl ether 5:1), to give adduct **14c** (211 mg, 0.87 mmol, 67%).

9-(2,4,6-Trimethylphenyl)-7-oxa-8-azadispiro[2.0.2.3]non-8-ene (14c): white solid, mp 110−111 °C, R_f 0.26; ^{1}H NMR δ 6.85 (s, 2H), 2.26 (s, 3H), 2.24 (s, 6H), 1.14−1.07 (m, 2H), 0.65−0.61 (m, 4H), 0.55−0.48 (m, 2H); ^{13}C NMR δ 163.0 (s), 138.9 (s), 137.3 (s, 2C), 128.3 (d, 2C), 123.6 (s), 68.5 (s), 34.3 (s), 21.1 (q), 19.5 (q, 2C), 8.7 (t, 2C), 8.3 (t, 2C); IR 3033, 2958, 2927, 1609, 1449, 1350 cm^{-1}; MS *m*/*z* 241 (M^+, 8), 240 (17), 226 (30), 212 (28), 198 (23), 184 (58), 170 (47), 145 (36), 144 (47), 130 (100), 119 (40), 115 (56), 103 (49), 91 (76). Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.66; H, 8.14; N, 5.46.

Cycloaddition of Nitrile Oxide 13d to Bicyclopropylidene (1). A solution of **1** (280 mg, 3.5 mmol) and **13d**[22] (856 mg, 3.0 mmol) in toluene (6 mL) was heated in a sealed tube at 110 °C for 7 d. The adduct **14d** (189 mg, 0.52 mmol, 17%) was collected by filtration of the precipitate formed by partial concentration *in vacuo* of the reaction mixture.

9-(Triphenylmethyl)-7-oxa-8-azadispiro[2.0.2.3]non-8-ene (14d): white solid, mp 186−187 °C, R_f 0.17 (petroleum ether−diethyl ether 9:1); ^{1}H NMR δ 7.40−7.15 (m, 15H), 1.13 (m, 2H), 0.52 (m, 2H), 0.22 (m, 2H), −0.10 (m, 2H); ^{13}C NMR δ 164.9 (s), 142.1 (s, 3C), 130.5 (d, 6C), 127.7 (d, 6C), 126.7 (d, 3C), 70.8 (s), 60.0 (s), 32.0 (s), 10.1 (t, 2C), 7.6 (t, 2C); IR 3088, 3065, 3023, 1596, 1491, 1446 cm^{-1}; MS *m*/*z* 365 (M^+, 0.6), 364 (1), 244 (13), 243 (91), 165 (100). Anal. Calcd for $C_{26}H_{23}NO$: C, 85.45; H, 6.34; N, 3.83. Found: C, 85.80; H, 6.63; N, 3.68.

Thermal Rearrangement of Adducts 14a and 14c: General Procedure. A solution of **14** (0.1 mmol) in *o*-dichlorobenzene (1 mL) was heated in a sealed tube at 170 °C for 5 d. The crude mixture was cooled to room temperature, and the solvent was removed by elution with petroleum ether through a short pad of silica gel. Compounds **18** were then eluted with petroleum ether−diethyl ether 3:8.

4-Phenyl-2,3-dihydrofuro[3,2-*c*]pyridine (18a): yield 44%, oil, R_f 0.33; ^{1}H NMR δ 8.41 (d, J = 5.5 Hz, 1H), 7.82−7.70 (m, 2H), 7.60−7.30 (m, 3H), 6.73 (d, J = 5.5 Hz, 1H), 4.65 (t, J = 8.6 Hz, 2H), 3.43 (t, J = 8.6 Hz, 2H); ^{13}C NMR δ 167.7 (s), 154.5 (s), 149.8 (d), 139.3 (s), 128.5 (d), 128.4 (d, 2C), 127.8 (d, 2C), 120.9 (s), 104.5 (d), 71.9 (t), 29.1 (t); IR 3080, 2928, 1585, 1571, 1496, 1457, 1430 cm^{-1}; MS *m*/*z* 197 (M^+, 85), 196 (100), 167 (29). Anal. Calcd for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10. Found: C, 79.00; H, 5.86; N, 6.67.

4-(2,4,6-Trimethylphenyl)-2,3-dihydrofuro[3,2-*c*]pyridine (18c): yield 44%, pale yellow solid, mp 81−83 °C, R_f 0.40; ^{1}H NMR δ 8.39 (d, J = 5.5 Hz, 1H), 6.91 (br s, 2H), 6.73 (d, J = 5.5 Hz, 1H), 4.63 (t, J = 8.8 Hz, 2H), 2.90 (t, J = 8.8 Hz, 2H), 2.31 (s, 3H), 2.00 (s, 6H); ^{13}C NMR δ 166.9 (s), 156.6 (s), 149.9 (d), 137.3 (s, 2C), 135.1 (s), 128.1 (d, 2C), 122.7 (s), 120.4 (s), 104.1 (d), 71.9 (t), 27.5 (t), 21.1 (q), 19.5 (q, 2C); IR 2924, 2858, 1583, 1448, 1374 cm^{-1}; MS *m*/*z* 239 (M^+, 31), 238 (52), 224 (100), 211 (40). Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 79.90; H, 7.18; N, 5.77.

One-Pot Reactions of Nitrile Oxides 13c,d with Bicyclopropylidene (1): General Procedure. A solution of an excess of BCP (**1**) and nitrile oxide (2 mmol) in *o*-dichlorobenzene (2.5 mL) was heated at 170 °C for 5 d. The reaction mixture was purified by direct flash chromatography on silica gel of the crude solution, eluting with petroleum ether to eliminate *o*-dichlorobenzene and then with the appropriate eluent.

4-(2,4,6-Trimethylphenyl)-2,3-dihydrofuro[3,2-*c*]pyridine (18c): yield 7%.

4-(Triphenylmethyl)-2,3-dihydrofuro[3,2-*c*]pyridine (18d): eluent petroleum ether−diethyl ether 2:1, R_f 0.44, pale yellow solid, mp 152−154 °C, yield 21%; ^{1}H NMR δ 8.32 (d, J = 5.5 Hz, 1H), 7.38−7.10 (m, 15H), 6.70 (d, J = 5.2 Hz, 1H), 4.29 (t, J = 8.8 Hz, 2H), 2.15 (t, J = 8.8 Hz, 2H); ^{13}C NMR δ 167.2 (s), 160.8 (s), 148.0 (s), 144.7 (d), 131.1 (d, 6C), 127.3 (d, 6C), 126.0 (d, 3C), 124.4 (s, 3C), 104.5 (d), 71.4 (t), 66.2 (s), 29.6 (t); IR 3062, 3033, 2976, 2928, 1596, 1568, 1491, 1445 cm^{-1}; MS *m*/*z* 363 (M^+, 16), 362 (11), 244 (29), 167 (23), 165 (38), 86 (66), 84 (100). Anal. Calcd for $C_{26}H_{21}NO$: C, 85.92; H, 5.82; N, 3.85. Found: C, 85.79; H, 6.14; N, 3.44.

Acknowledgment. This work was supported by the MURST and CNR (Italy), the Fonds der Chemischen Industrie, and BASF, Bayer, Degussa, Hoechst, and Hüls AG (chemicals). The authors are indebted to CRUI-Italy (Conferenza dei Rettori delle Università Italiane) and the German Academic Exchange Service (DAAD) for additional financial support of this collaborative project within the Vigoni Program.

JO951838L

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