Chameleon Thermal Behavior of Cycloadducts of Nitrones to Methyl 2-Chloro-2-cyclopropylidene- and 2-Chloro-2-spiropentylideneacetates

Chiara Zorn,[†] Andrea Goti,[†] Alberto Brandi,*[,†] Keyji Johnsen,[‡] Mathias Noltemeyer,[‡] Sergei I. Kozhushkov,[§] and Armin de Meijere*[,§]

Dipartimento di Chimica Organica "U. Schiff", and Centro di Studio sulla Chimica e la Struttura dei Composti Eterociclici e loro Applicazioni, C.N.R., Università di Firenze, Via G. Capponi 9, I-50121 Firenze, Italy, Institut für Anorganische Chemie der Georg-August-Universität Göttingen, Tammannstrasse 4, D-37077 Göttingen, Germany, and Institut für Organische Chemie der Georg-August-Universität Göttingen, Tammannstrasse 2, D-37077 Göttingen, Germany

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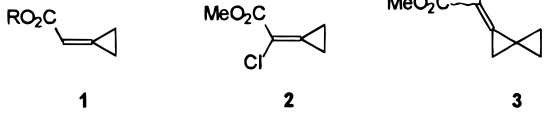
Methyl 2-chloro-2-cyclopropylideneacetate (**2**) and its spiropentane analogue **3** cycloadd to dihydroisoquinoline *N*-oxide (**9**), pyrroline *N*-oxide (**12**), and *C*-phenyl-*N*-methylnitrone (**16**) to give 5-spirocyclopropaneisoxazolidines in good yields (58−93%). The thermal behavior of the 5-spirocyclopropaneisoxazolidines is rather differentiated, depending strongly on the constitution of the nitrone and the solvent. As nitrone **9** has the tendency to undergo cycloreversion reactions, the ketoamide rearrangement products **20** and **21** from its cycloadduct derive from the thermodynamically favored 4-spirocyclopropaneisoxazolidine regioisomers formed after the cycloreversion process. In DMSO as solvent different rearrangement processes take place, leading to benzoindolizinones in modest yields (15−21%). The cycloadducts from **12** and **16** undergo a cyclopropyl to cyclobutyl ring enlargement facilitated by the presence of a chlorine substituent on the carbon α to the spirocyclopropane ring. Whereas these compounds from nitrone **16** demonstrated an unusual stability, those from nitrone **12** undergo a cascade rearrangement to yield indolizinone derivatives **34**, **35** cleanly (73−83% yield). This overall transformation offers a new method for the synthesis of the indolizine skeleton.

Introduction

The chemistry of methylene- and alkylidenecyclopropanes has flourished in the past decade. The wide and diversified application of these compounds in organic synthesis is well documented in comprehensive reviews which recently appeared.[1] Among the functionally substituted substrates in this family, the cyclopropylideneacetates **1** with an alkoxycarbonyl group at the exocyclic carbon−carbon double bond can easily be obtained by acid-catalyzed Wittig olefination of the cyclopropanone hemiacetal.[2]



1 **2** **3**

The alkoxycarbonyl group in **1**, besides playing the role of activating the double bond toward additions, in nitrone 1,3-dipolar cycloadditions provides a high control of the regioselectivity leading to the formation of 4-alkoxycarbonyl-substituted (isoxazoline numbering) isoxazolidines.[3] Methyl 2-chloro-2-cyclopropylideneacetate (**2**) is a particularly useful, since highly functionalized, building block which is easily available in multigram quantities.[4] It is a highly reactive Michael acceptor which adds a large variety of nucleophiles including dienolates, the latter generating complex tricyclic skeletons in high yields.[5] The addition of appropriate nitrogen nucleophiles to **2** yields precursors to various α- and *β*-amino acids.[6] The α-chloroacrylate **2** also proved to be a reactive dienophile.[4a,7] Methyl 2-chloro-2-spiropentylideneacetate (**3**)[8] is a less well developed reagent, but also easily accessible from methylenecyclopropane along a route analogous to that

[†] Università di Firenze. Email: brandi@chimorg.unifi.it.

[‡] Institut für Anorganische Chemie der Georg-August-Universität Göttingen.

[§] Institut für Organische Chemie der Georg-August-Universität Göttingen. Email: ameijer1@uni-goettingen.de.

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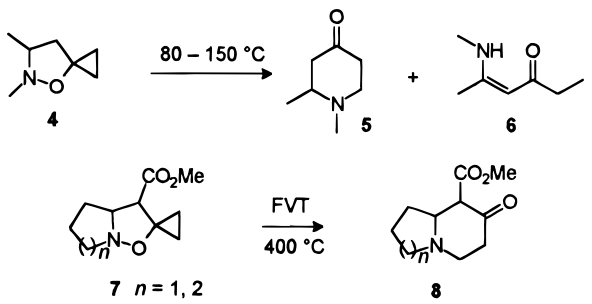
Scheme 1



leading to **2**. The more highly strained **3** is even more reactive in Michael additions and cycloadditions.[8,9]

1,3-Dipolar cycloadditions to compounds **2** and **3** have so far received only scarce attention, limited to one example each of a cycloaddition of diphenyldiazomethane and of a nitrile ylide to **2**.[4c] In view of the rich chemistry originating from the thermal rearrangement of the 5-spirocyclopropaneisoxazolidines **4**[10] deriving from cycloadditions of nitrones to methylenecyclopropanes, we investigated the nitrone cycloadditions to **2** as well as **3** and the thermal transformation of their cycloadducts. The thermal rearrangement of 5-spirocyclopropaneisoxazolidines **4**, commonly carried out by heating a dilute solution of the compound in an appropriate solvent, leads, in general, to cyclic tetrahydropyridones **5** besides minor amounts of enaminones **6** as side products (Scheme 1).

The temperature required to initiate the rearrangement of compounds of type **4** ranges from 80 to 150 °C. However, when the substrate carries a methoxycarbonyl group at the 4-position as in the isoxazolidine **7** (Scheme 1) the required temperature is much higher.[3] In such cases, FVT (flash vacuum thermolysis) conditions are preferable to avoid competing decomposition processes, either of the reagent or of the product. It looks as though the CO_2Me group exerts a stabilization of the 5-spirocyclopropaneisoxazolidine, an effect which is far from being understood. It appeared that the study of the thermal rearrangement of spirocyclopropaneisoxazolidines carrying both a chlorine and a methoxycarbonyl substituent might also add some clue to the understanding of the role of substituents on the rearrangement step.

Results and Discussion

1,3-Dipolar Cycloadditions. The results of the cycloadditions of nitrones **9**, **12**, and **16** to **2** and **3** are shown in Table 1. All cycloadditions were carried out under mild conditions (ambient temperature, 40 or 60 °C, 1.5−60 h) affording good yields of cycloadducts **10**, **11**, **13**, **14**, and **17**−**19**.

The cycloadditions of endocyclic nitrones **9**, **12** (entries 1−4) were diastereoselective, proceeding exclusively via the *endo*-methoxycarbonyl approach, most likely favored by secondary orbital interactions, of the cyclic nitrones with the alkene to give the trans-{H/CO_2Me} cycloadducts. The formation of an inseparable mixture of two diastereoisomers **11** (entry 2) originated from the fact that a mixture of (*E*)- and (*Z*)-acetate **3** was used. Nitrone **16** (entry 5) gave a 5:1 mixture of diastereoisomers **17** and **18**; the lower selectivity, however, could derive from the nitrone which equilibrates between the (*E*)- and (*Z*)-configurations at the reaction temperature. The major isomer was tentatively assigned the structure **17** with *cis*-{Ph/CO_2Me} relationship on the basis of the high field shift observed for the proton 3-H (δ = 4.41 in **17** versus 4.79 ppm in **18**). The same nitrone **16** reacted with (*Z*)-**3** to give one single diastereoisomer **19**, with a configuration analogous to that of **17**, probably due to the major steric hindrance inferred by the spiropentylidene group. Nitrone **12** gave with (*Z*)-**3** a single cycloadduct **14** (58%) besides compound **15**, derived from **14** by a subsequent rearrangement (see below), in 12% yield (entry 4). The structural assignments of the adducts were unequivocally made on the basis of their ^{1}H and ^{13}C NMR spectra. They show characteristic signals of the cyclopropane protons (δ 1.8−0.8 ppm) and the proton 3-H in the isoxazolidine ring (singlets at δ = 5.50, 5.58, 4.41, 4.79, and 5.00 ppm for **10**, **11**, **17**, **18**, and **19**, respectively; triplets at δ = 4.16 and 4.12 ppm for **13** and **14**, respectively). The configuration of the cycloadduct **10** was confirmed by an X-ray crystal structure analysis (Figure 1).

Thermal Rearrangements. Isoxazolidines **10** and **11** turned out to be quite stable at temperatures below 100 °C. When heated at 150 °C in xylene they underwent a clean rearrangement, but did not give any of the expected product related to **5** or **6** (Scheme 2).

The ketoamide **20** was obtained from **10** in 56% yield. Assignment of the structure was not trivial on the basis of spectra, albeit signals of an enamine moiety (^{13}C NMR: δ = 158.6 and 104.9 ppm) and carbonyl and amide carbons (^{13}C NMR: δ = 185.0 and 157.2 ppm) were quite diagnostic along with the lack of the MeO carbon signal. An X-ray analysis was necessary to unequivocally confirm the structure of the product to be **20** (Figure 2).

Compound **11** underwent an analogous rearrangement, but, under the same conditions, afforded a mixture (ratio 1:2.5) of the corresponding ketoamide **21** and the ketoester **22** as the major product (Scheme 2). Prolonged heating of the reaction mixture gave compounds **21** and **22** in an almost inverted ratio, but accompanied by abundant decomposition products. The structural assignment for **21** was guided by the observation of diagnostic signals for the MeO_2C group in the NMR spectra and the singlet of the proton α to the C=O group (^{1}H NMR: δ = 4.00 ppm). The connectivity between the functional groups was confirmed on the basis of the ^2J and ^3J coupling constants observed in a COLOC-2D NMR spectrum. It is obvious that **22** must be the direct precursor of **21** which would be formed from **22** via its enamine tautomer. The fact that it could be isolated in this case, and not in the rearrangement of **10**, must have to do with the added spirocyclopropane ring which must

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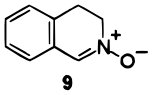
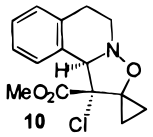
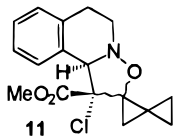
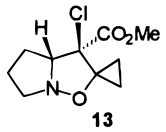
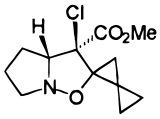
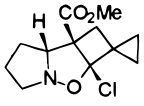
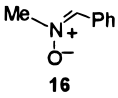
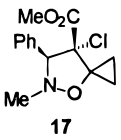
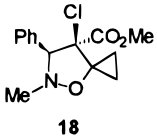
Table 1. Cycloadditions of Nitrones 9, 12, and 16 to 2-Chloro-2-cyclopropylidene- (2) and 2-Chloro-2-spiropentylideneacetate (3)

Entry	Alkene	Nitrone	Reaction Conditions	Cycloadducts	Yield (%)
1	2	 9	CH_2Cl_2 38 °C, 2 h	 10	91
2	(*Z*,*E*)-3	9	CH_2Cl_2 38 °C, 2 h	 11	93
3	2	 12	CH_2Cl_2 25 °C, 60 h	 13	65
4	(*Z*)-3	12	CH_2Cl_2 25 °C, 60 h	 14  15	58 **14** 12 **15**
5	2	 16	Toluene 60 °C, 36 h	 17  18	70 **17** 13 **18**
6	(*Z*)-3	16	Toluene 60 °C, 5 h	 19	68

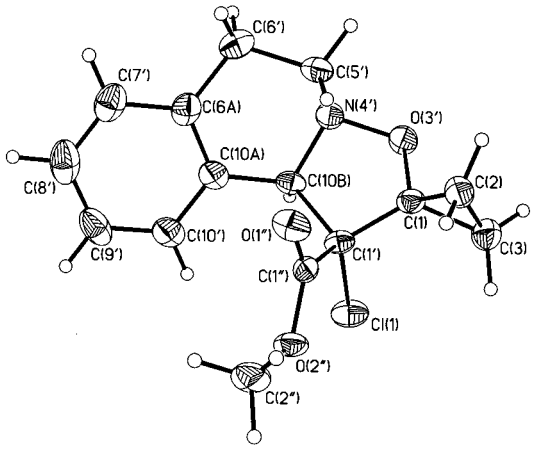
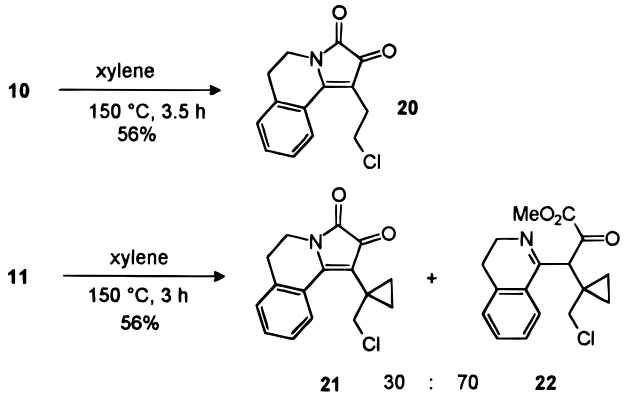


Figure 1. Crystal structure of cycloadduct **10**.

Scheme 2



imply a higher total strain for compound **20**. The formation of compounds **20**−**22** can be rationalized only assuming that the primary cycloadducts **10**, **11** undergo a cycloreversion−recycloaddition sequence finally leading to the thermodynamically more stable cycloadducts **23**, **24** (Scheme 3). As a matter of fact, cycloreversion reactions[11] are common in 1,3-dipolar cycloaddition chemistry. An important factor that facilitates the cycloreversion of isoxazolidines is the conjugative and electron-withdrawing effect of substituents at the double bond being reformed, as in the case of acrylates **2** and **3**. Once the cycloaddition−cycloreversion equilibrium is estab-

(11) Bianchi, G.; Gandolfi, R. 1,3-Dipolar Cycloreversions. In *1,3-Dipolar-Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 2.

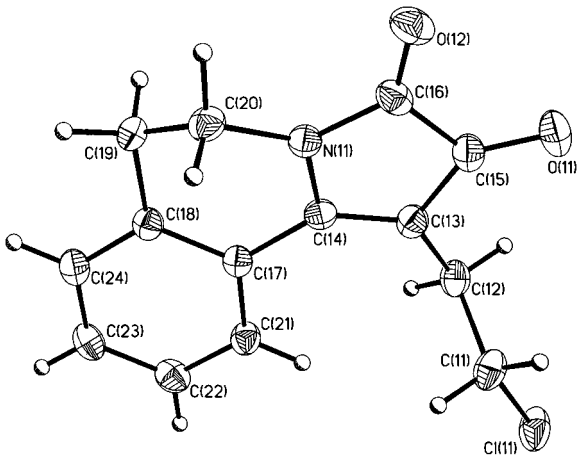
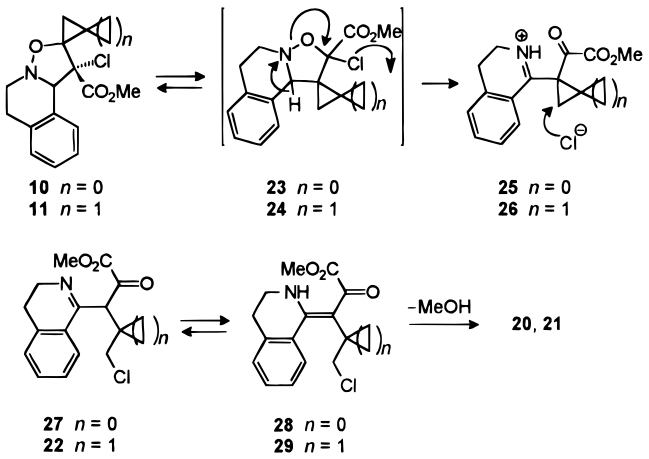


Figure 2. Crystal structure of compound **20**.

Scheme 3



10 $n = 0$ **11** $n = 1$ **23** $n = 0$ **24** $n = 1$ **25** $n = 0$ **26** $n = 1$

27 $n = 0$ **22** $n = 1$ **28** $n = 0$ **29** $n = 1$ **20, 21**

lished, a mixture of cycloadducts based on their relative thermodynamic stability originates. The 4-spirocyclopropaneisoxazolidines **23**, **24**, which must form in these processes, can undergo a sequential ring opening followed by nucleophilic attack of chloride on the bisacceptor-substituted cyclopropane ring in **25**, **26** to form the α-ketoester **27**, **22**, one of which was actually isolated, namely **22** for the case of $n = 1$ (Scheme 3). The enamine tautomers **28**, **29** then undergo cyclization with loss of methanol.

The 4-spirocyclopropaneisoxazolidines **23**, **24** could not be detected in the reaction mixtures after heating **10**, **11** in xylene. Upon heating the cycloadducts **10** and **11** in toluene solutions at 110 °C for 3 h, however, equilibrium mixtures of two diastereromeric cycloadducts were obtained in which the thermodynamically more stable isoxazolidines **30** and **31** predominated by factors of 8:1 and 2.5:1, respectively (Scheme 4). Apparently, the recycloaddition at this temperature gave the same regioisomeric product, but occurred in an *exo*-{CO_2Me} mode (Scheme 4) as was proved by an X-ray crystal structure analysis of compound **30** (Figure 3) which unequivocally proved that it has the *exo*-{CO_2Me} configuration in contrast to isomer **10** with its *endo*-{CO_2Me} orientation (Figure 1). By analogy of its NMR spectra the structure of compound **31** could be assigned as being completely analogous. The 4-spirocyclopropaneisoxazolidines **23**, **24** then must form at higher temperatures, at which they immediately undergo the rearrangement depicted in Scheme 3.

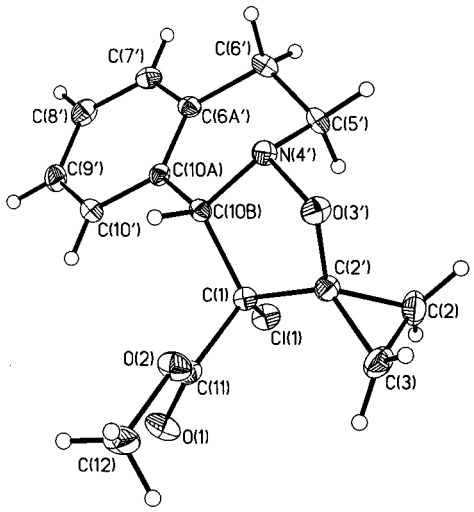
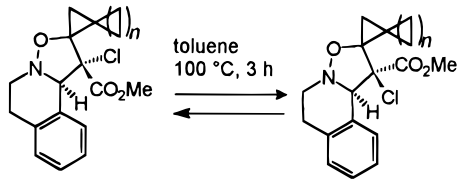


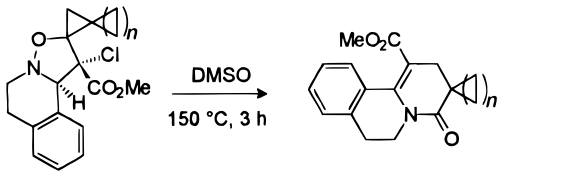
Figure 3. Crystal structure of thermodynamic cycloadduct **30**.

Scheme 4



10 $n = 0$ **11** $n = 1$ **30** + **10** (8:1) $n = 0$ **31** + **11** (2.5:1) $n = 1$

Scheme 5

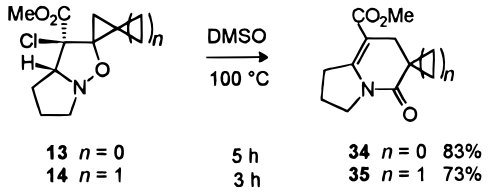


10 $n = 0$ **11** $n = 1$ **32** $n = 0$ 15% + **20** 8% **33** $n = 1$ 21%

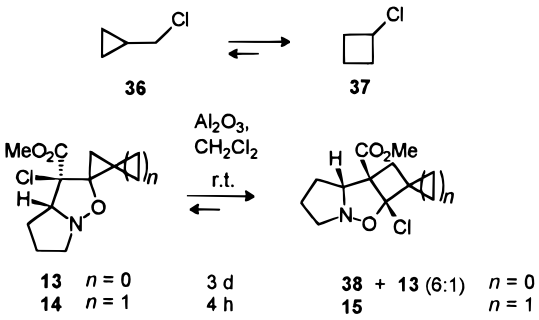
When the thermal rearrangement was carried out in DMSO at 150 °C a completely different reaction pathway of isoxazolidines **10**, **11** was observed. Albeit decomposition of the starting materials predominated, the benzoquinolizinones **32** and **33** were isolated in 15 and 21% yield, respectively (Scheme 5). Benzoquinolizinone **32** was obtained as an unseparable mixture together with the ketoamide **20** (8%).

The structural assignment was not straightforward, lacking the possibility of establishing the connectivity from coupling patterns between protons. However, the lack of a chlorine substituent as established by the mass spectrum and the presence of an amide and an α,β-unsaturated ester functionality as evidenced by the ^{13}C NMR spectrum were sufficiently diagnostic to elucidate the unexpected structure. The structural assignment and the origin of the new products became clear after studying the rearrangements of the other cycloadducts from pyrroline *N*-oxide (**12**) and *C*-phenyl-*N*-methylnitrone (**16**). When the isoxazolidines **13** and **14** were heated at 110 °C in toluene as commonly done for thermal rearrangements of spirocyclopropaneisoxazolidines,[10] complex

Scheme 6



Scheme 7

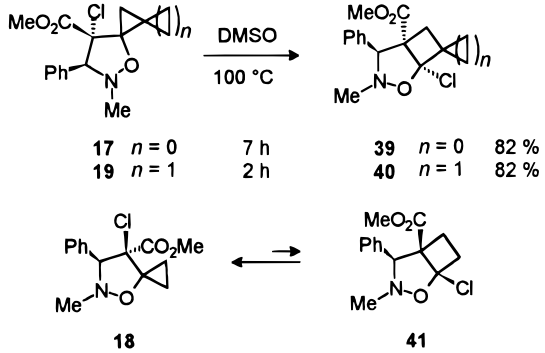


mixtures of products were obtained and no trace of compounds such as **20**−**22** was observed in the reaction mixtures.

However, by heating **13** and **14** in the more polar DMSO at 100 °C, a clean and fast reaction occurred to give the hexahydroindolizin-5-ones **34**[12] and **35** in 83 and 73% yield, respectively (Scheme 6).[13] As these compounds were present only in minute amounts in the heated toluene solutions, it is obvious that the polarity of the solvent plays a key role in controlling the rearrangement process. The amide carbon signals in the ^{13}C NMR spectra of **34** (δ = 167.8 ppm) and **35** (δ = 167.5 ppm) suggested that indolizidin-5-ones were obtained instead of the common indolizidine-7-ones **8**, and that a new mechanism was in action. The apparent influence of the polar solvent suggested that a charge separation played a role on going to the transition state. The presence of a chlorine α to a cyclopropane ring in the isoxazolidines **13** and **14** suggested that in each case the cyclopropylmethyl chloride moiety was equilibrating with a cyclobutyl chloride substructure[14] (Scheme 7) under these conditions in a polar solvent like DMSO that favors the heterolytic cleavage of a C−Cl bond.

The equilibrium between **36** and **37** in most cases favors the cyclobutyl derivative for reasons of strain relief, and the rearrangement is catalyzed by Lewis acids. A more careful analysis of the reaction mixture from the cycloaddition of **12** to (*Z*)-**3** showed that, in fact, even at room temperature after an extended time (60 h) in methylene chloride solution, a 12% yield of the cyclobutane-annelated isoxazolidine **15** was obtained (Table 1, entry 4). When a solution of the isoxazolidine **14** in

Scheme 8



CH_2Cl_2 was stirred in the presence of the mildly Lewis acidic Al_2O_3, the transformation to **15** occurred much more rapidly and was complete within 4 h at ambient temperature. Similar treatment of **13** gave the cyclobutane-annelated derivative **38** as the major product (86% of **38** besides 14% of **13**) after 3 days (Scheme 7).

Compounds **38** and **15** turned out to be quite sensitive to purification procedures, particularly column chromatography; this must be a consequence of the peculiar neighborhood relationship of functional groups on top of the ring strain incorporated in these compounds. Nevertheless, all spectroscopic data were in accord with the proposed structure. The configurations could be assigned only tentatively, but they are consistent with an S_N2 process with the 1,2-migrating C,C-bond replacing the chloride at C-4 (isoxazolidine numbering) and thus enforcing the cis-{H,CO_2Me} relationship on the two neighboring bridgeheads. The attack of the chloride on the cyclobutyl cation can then occur only on the convex face of the molecule affording the all-cis relationship of the substituents on all three bridgehead positions.

The best confirmation for the mechanism of this rearrangement and its stereochemical implications came, indirectly, from the outcome of the thermal isomerization of the diastereomeric isoxazolidines **17** and **18**. When the diastereomeric mixture **17**/**18** was heated in DMSO under the same conditions as applied for **13** and **14** (Scheme 6) for 7 h, the major diastereomer **17** had disappeared, and rearranged quantitatively (82% isolated yield) to a crystalline product identified as the cyclobutane-annelated isoxazolidine **39** (Scheme 8). The minor diastereomer **18** was recovered intact by chromatographic separation. Spiropentylidene derivative **19** under the same conditions gave the analogous cyclobutane-annelated isoxazolidine **40**. Compounds **39** and **40** presented all the characteristic spectroscopic features observed for the analogous compounds **38** and **15**, yet in addition an X-ray crystal structure analysis (Figure 4) proved the relative configuration of **39** and thus strongly corroborated the configurational assignments made for all the other derivatives of this type.

Thus the crystal structure of **39** also confirmed all the mechanistic implications discussed for the rearrangements of **13** and **14** to **38** and **15**, and in addition makes it possible to explain why the minor isomer **18** does not undergo this type of rearrangement. If such a rearrangement of **18** with an S_N2 displacement of the chloride would occur, it would place the Ph and the CO_2Me groups in an unfavorable cis relationship on the bicyclic isoxazolidine **41** (Scheme 8). Since the overall process must be reversible, the equilibrium in this case is shifted all

(12) (a) Célérier, J.-P.; Eskénazi, C.; Lhommet, G.; Maitte, P. *J. Heterocycl. Chem.* **1979**, *16*, 953−955. (b) Brunerie, P.; Célérier, J.-P.; Huché, M.; Lhommet, G. *Synthesis* **1985**, 735−738. (c) Paulvannan, K.; Stille, J. R. *Tetrahedron Lett.* **1993**, *34*, 8197−8200. (d) Paulvannan, K.; Stille, J. R *J. Org. Chem.* **1994**, *59*, 1613−1620.

(13) Preliminary communication: Zorn, C.; Goti, A.; Brandi, A.; Johnsen, K.; Kozhushkov, S. I.; de Meijere, A. *Chem. Commun.* **1998**, 903−904.

(14) (a) Caserio, M. C.; Graham, W. H.; Roberts, J. D. *Tetrahedron* **1960**, *11*, 171−182. (b) Roberts, J. D.; Mazur, R. H. *J. Am. Chem. Soc.* **1951**, *73*, 2509−2520. (c) Renk, E.; Roberts, J. D. *J. Am. Chem. Soc.* **1961**, *83*, 878−879. (d) Klunder, A. J. M.; Zwanenburg, B. In *Houben-Weyl Vol. E17c*; de Meijere, A., Ed.; Thieme: Stuttgart, 1997; pp 2419−2437.

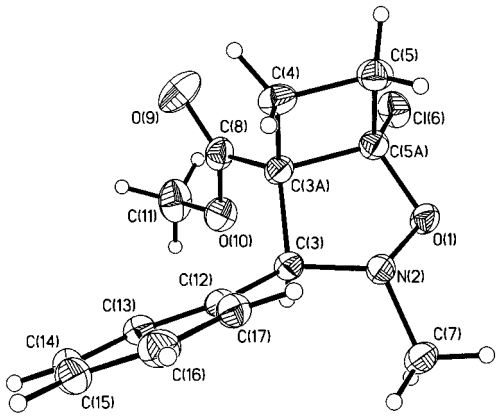
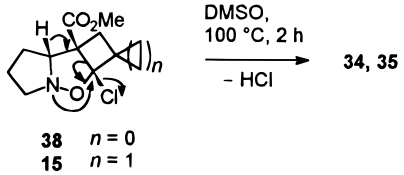


Figure 4. Crystal structure of compound **39**.

Scheme 9



the way toward the spirocyclopropane derivative **18** rather than the cyclobutyl chloride **41**.

The 3-aza-2-oxabicyclo[3.2.0]heptane derivatives **39** and **40** exhibited an extraordinary stability of their skeleton toward further thermal rearrangement and other chemical transformations. They are stable toward $NaBH_4$ and $LiAlH_4$ at room temperature. Heating of **39** and **40** in *o*-dichlorobenzene, xylene, or DMSO up to 160 °C left the compounds only partially decomposed. On the other hand, the analogous tricyclic cyclobutane derivatives **38** and **15** behave quite differently. When heated in DMSO at 100 °C for 2 h, they were transformed quantitatively to the same indolizidin-5-ones **34** and **35** just like the isoxazolidines **13** and **14**. Compounds **38** and **15**, therefore, most probably are the intermediates en route from **13** and **14** to **34** and **35**. The indolizidin-5-ones **34** and **35** must form by a ring-enlargement process that is unprecedented to the best of our knowledge (Scheme 9).

Conclusion

In the reported 1,3-dipolar cycloadditions of nitrones to the functionally substituted methylenecyclopropane derivatives **2** and **3** the chlorine atom in the dipolarophiles plays a key role and, by its nature of being a good leaving group, confers to the isoxazolidine adducts the possibility to undergo unprecedented types of ring reorganization which are made selective by the concomitant presence of an α-spiroannelated cyclopropane ring. The constitution of the nitrone also plays an important role, as it determines the tendency to undergo cycloreversion reactions, known to be higher for cycloadducts of nitrone **9**,[11] and this in turn determines the outcome of the rearrangement process. Finally, the solvent polarity can be decisive, as more polar solvents, in connection with the presence of a chloride leaving group, can stabilize polar intermediates. This was observed here for the first time in the chemistry of 5-spirocyclopropaneisoxazolidines.[10] Such polar intermediates, e. g. derived from isoxazolidines **13** and **14**, can lead to completely new processes with the selective and very efficient formation of new tetrahydro-1*H*-indolizin-5-ones **34** and **35**. This study has also allowed the isolation and characterization (including an X-ray crystal structure analysis) of novel tricyclic and bicyclic cyclobutane-annelated isoxazolidines **15** and **38**−**40** bearing a chlorine substituent on a bridgehead carbon atom α to an oxygen. The surprising stability, at least of compounds **39** and **40** despite their remarkable structural features, deserves further investigations of these and related compounds which should disclose other possible synthetic applications. The application of the reported new and easy access to indolizinones toward the synthesis of natural product targets is currently being considered in our laboratories.

Experimental Section

^1H and ^{13}C NMR spectra were recorded at 200 (^1H) and 50 MHz [^{13}C, additional APT (attached proton test)] in $CDCl_3$ solution, if not otherwise specified. MS (EI) were recorded at 70 eV by GC inlet or by direct inlet and MS (HR-EI) at 70 eV (preselected ion peak matching at $R \gg 10000$ to be within ±2 ppm of the exact masses).

(1′*R,10b′*R**)-1′-Chloro-1′-(methoxycarbonyl)-6′,10′-dihydrospiro[1,2′-cyclopropane-(5′*H*)-[2*H*]isoxazolo[3,2-*a*]-isoquinoline] (10).**[15] A solution of the ester **2** (30 mg, 0.205 mmol) and nitrone **9** (40 mg, 0.27 mmol) in CH_2Cl_2 (0.5 mL) was heated in a sealed tube for 1.5 h at 38 °C. The solvent was removed in vacuo, and flash column chromatography of the resulting mixture on aluminum oxide (eluent petroleum ether/CH_2Cl_2/EtOAc 5:5:1) afforded cycloadduct **10** (53 mg, 88%) as a solid, mp 82−84 °C (CH_2Cl_2/petroleum ether), R_f = 0.55. ^1H NMR: δ 7.31−7.22 (m, 1 H), 7.19−7.13 (m, 3 H), 5.50 (s, 1 H), 3.39 (td, J = 6.2, 10.9 Hz, 1 H), 3.28 (s, 3 H) 3.38−3.17 (m, 1 H), 3.09 (dt, J = 14.9, 5.2 Hz, 1 H), 2.94−2.85 (m, 1 H), 1.47−1.36 (m, 1 H) 1.30−1.22 (m, 1 H), 1.18−1.05 (m, 2 H). ^{13}C NMR: δ 167.3 (s), 133.7 (s), 131.0 (s), 128.0 (d), 127.7 (d), 126.0 (d), 125.8 (d), 85.0 (s), 77.5 (d), 73.3 (s), 53.0 (q), 47.1 (t), 28.5 (t), 19.6 (t), 9.2 (t). IR (CH_2Cl_2): 3062, 2958, 1743, 1419 cm^{-1}. MS: *m*/*z* (rel intensity) 295 (M^+, 5), 293 (M^+, 14), 262 (4), 158 (100), 147 (47), 131 (92), 77 (7), 59 (6). HRMS: 293.0818.

(1″*R,10b″*R**)-1″-Chloro-1″-(methoxycarbonyl)-6″,10″-dihydrodispiro[cyclopropane-1,1′-cyclopropane-2′,2″-(5″*H*)-[2*H*]isoxazolo[3,2-*a*]isoquinoline] (11).** A solution of the ester **3** (*E*/*Z* mixture) (64 mg, 0.37 mmol) and nitrone **9** (58 mg, 0.39 mmol) in CH_2Cl_2 (1 mL) was heated in a Sovirel tube (a Pyrex tube sealed with a screw cap) for 1.5 h at 38 °C. The solvent was removed in vacuo, and flash column chromatography (Al_2O_3, eluent: petroleum ether/CH_2Cl_2/ethyl acetate 5:5:1) of the resulting mixture afforded cycloadduct **11** (110 mg, 93%) as a solid mixture of two diastereoisomers (1:1 ratio according to ^{13}C NMR) not separable by TLC. R_f = 0.61. ^1H NMR: δ 7.26−7.21 (m, 1 H), 7.19−7.16 (m, 3 H), 5.58 (s, 1 H), 4.02 (ddd, J = 11.8, 9.1, 4.0 Hz, 1 H), 3.32 (s, 3 H), 3.38−3.25 (m, 1 H), 3.20−3.03 (m, 1 H), 2.93−2.85 (m, 1 H), 1.75−1.49 (m, 2 H), 1.37 (d, J = 5.9 Hz, 1 H), 1.16−1.07 (m, 1 H), 0.99−0.83 (m, 2 H). ^{13}C NMR: (first diastereoisomer) δ 167.2 (s), 133.7 (s), 131.1 (s), 128.0 (d), 127.7 (d), 126.0 (d), 125.6 (d), 85.0 (s), 79.4 (d), 75.4 (s), 53.0 (q), 47.4 (t), 28.7 (t), 24.2 (t), 15.8 (s), 7.2 (t), 4.9 (t); (second diastereoisomer) δ 166.3 (s), 133.5 (s), 131.0 (s), 127.9 (d), 127.5 (d), 125.9 (d), 81.4 (d), 73.7 (s), 52.65 (q), 46.8 (t), 27.9 (t), 22.9 (t), 6.1 (t), 4.5 (t). IR (CH_2Cl_2): 3053, 3003, 2955, 2901, 1745, 1528, 1494 cm^{-1}. MS: *m*/*z* (rel intensity) 318 (5), 284 (14), 157 (13), 147 (100), 131 (28), 130 (52), 115 (18). HRMS: 319.0975.

(15) The authors have deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. X-ray structural data have been deposited with the Cambridge crystallographic data file.

(3′*S,3a′*S**)-3′-Chloro-3′-(methoxycarbonyl)tetrahydrospiro[cyclopropane-1,2′(3′*H*)-pyrrolo[1,2-*b*]isoxazole] (13).** A solution of the ester **2** (426 mg, 2.91 mmol) and nitrone **12** (300 mg, 3.53 mmol) in CH_2Cl_2 (7 mL) was stirred under nitrogen at room temperature for 60 h. The solvent was removed in vacuo, and flash column chromatography (Al_2O_3, eluent petroleum ether/CH_2Cl_2/ethyl acetate 1:1:1) of the resulting mixture afforded cycloadduct **13** (435 mg, 65%) as a yellow oil, R_f = 0.44. ^{1}H NMR: δ 4.16 (t, J = 7.7 Hz, 1 H), 3.75 (s, 3 H), 3.38−3.08 (m, 2 H), 2.14−1.87 (m, 2 H), 1.86−1.59 (m, 2 H), 1.40−1.33 (m, 1 H), 1.26−1.12 (m, 1 H), 1.09−1.00 (m, 2 H). ^{13}C NMR [$(CD_3)_2CO$]: δ 166.6 (s), 78.8 (s), 77.2 (d), 67.2 (s), 57.8 (t), 52.9 (q), 30.6 (t), 24.8 (t), 16.0 (t), 6.5 (t). IR (CH_2Cl_2): 2958, 1746, 1441 cm^{-1}. MS: *m*/*z* (rel intensity) 233 (M^+, 7), 231 (M^+, 21), 198 (20), 164 (73), 154 (34), 147 (28), 96 (90), 82 (37), 69 (53), 59 (49), 55 (60), 53 (54), 42 (80), 41 (100). Anal. Calcd for $C_{10}H_{14}ClNO_3$ (231.7): C, 51.84; H, 6.09; N, 6.05. Found: C, 51.98; H, 6.25; N, 5.80.

(3″*S,3″a*S**)-3″-Chloro-3″-(methoxycarbonyl)tetrahydrodispiro[cyclopropane-1,1′-cyclopropane-2′,2″(3″*H*)-pyrrolo[1,2-*b*]isoxazole (14) and Methyl Spiro[cyclopropane-1′,4-(3-chloro-1-aza-2-oxatricyclo[5.3.0.0^{3,6}]decane-6-carboxylate)] (15).** A solution of the ester (*Z*)-**3** (300 mg, 1.74 mmol) and nitrone **12** (300 mg, 3.53 mmol) in CH_2Cl_2 (8 mL) was stirred under nitrogen at room temperature for 60 h. The solvent was removed in vacuo, and flash column chromatography (Al_2O_3, eluent diethyl ether) of the resulting mixture afforded an unseparable mixture of cycloadduct **14** and compound **15** (315 mg, 70%, **14**:**15** 5:1 according to ^{1}H NMR), **14**: R_f = 0.49. ^{1}H NMR: δ 4.12 (t, J = 7.7 Hz, 1 H), 3.75 (s, 3 H), 3.46−3.32 (m, 1 H), 3.24−3.08 (m, 1 H), 2.11−1.83 (m, 2 H), 1.82−1.60 (m, 2 H), 1.34−1.15 (m, 2 H), 1.05−0.72 (m, 4 H). ^{13}C NMR: δ 165.7 (s), 78.0 (s), 76.90 (d), 68.8 (s), 58.0 (t), 52.5 (q), 30.1 (t), 24.5 (t), 20.2 (t), 12.8 (s), 5.4 (t), 4.4 (t). IR ($CDCl_3$): 2957, 1747, 1437 cm^{-1}. MS: *m*/*z* (rel intensity) 259 (M^+, 2), 257 (M^+, 7), 221 (16), 206 (48), 162 (79), 157 (30), 134 (27), 86 (57), 70 (65), 59 (51), 53 (100).

(6*S,7*S**)- and (6*S**,7*R**)-7-Chloro-6-phenyl-5-methyl-7-(methoxycarbonyl)-4-oxa-5-azaspiro[2.4]heptane (17 and 18).** A solution of the ester **2** (348 mg, 2.37 mmol) and nitrone **16** (480 mg, 3.53 mmol) in toluene (3 mL) was heated in a Sovirel tube for 36 h at 60 °C. The solvent was removed in vacuo, and flash column chromatography (silica gel, eluent petroleum ether/ethyl acetate 5:1) afforded the diastereomeric cycloadducts **17** (470 mg, 70%) and **18** (90 mg, 13%) as solids.

17: Mp 90−92 °C (ethyl acetate/petroleum ether), R_f = 0.27. ^{1}H NMR: δ 7.50−7.40 (m, 2 H), 7.38−7.33 (m, 3 H), 4.41 (s, 1 H), 3.38 (s, 3 H), 2.78 (s, 3 H), 1.40 (ddd, J = 11.3, 6.2, 3.7 Hz, 1 H), 1.27−1.00 (m, 3 H). ^{13}C NMR: δ 166.7 (s), 133.5 (s), 128.8 (d), 128.3 (d), 127.9 (d), 87.2 (d), 82.1 (s), 70.8 (s), 52.8 (q), 44.0 (q), 16.6 (t), 11.6 (t). IR (CH_2Cl_2): 3070, 2955, 1745, 1605, 1435 cm^{-1}. MS: *m*/*z* (rel intensity) 283 (M^+, 1), 281 (M^+, 3), 160 (26), 145 (59), 131 (36), 118 (100). Anal. Calcd for $C_{14}H_{16}ClNO_3$ (281.7): C, 59.68; H, 5.72; N, 4.97. Found: C, 59.95; H, 5.71; N, 4.71.

18: R_f = 0.45, ^{1}H NMR: δ 7.48−7.39 (m, 2 H), 7.37−7.31 (m, 3 H), 4.79 (s, 1 H), 3.80 (s, 3 H), 2.71 (s, 3 H), 1.30−1.09 (m, 3 H), 1.00−0.87 (m, 1 H). ^{13}C NMR: δ 168.7 (s), 134.8 (s), 130.0 (d), 129.1 (d), 128.5 (d), 81.2 (d), 80.36 (s), 71.6 (s), 53.9 (q), 44.3 (q), 13.4 (t), 12.3 (t). MS: *m*/*z* (rel intensity) 283 (M^+, 1), 281 (M^+, 3), 146 (61), 131 (20), 118 (100), 77 (38), 42 (67).

(5*S,8*S**,9*S**)-9-Chloro-8-phenyl-7-methyl-9-(methoxycarbonyl)-7-aza-6-oxadispiro [2.2.4]nonane (19).** A solution of the ester (*Z*)-**3** (220 mg, 1.28 mmol) and nitrone **16** (197 mg, 1.45 mmol) in toluene (5 mL) was heated in a sealed tube for 5 h at 60 °C. The solvent was removed in vacuo, and filtration of the resulting mixture on Al_2O_3 (pH 9.5), eluent: petroleum ether/ethyl acetate 5:1, afforded the cycloadduct **19** (268 mg, 68%) as a diastereomerically pure oil. Product **19** cannot be obtained pure for elemental analysis because the more it remains in solution the more it turns into **40**, and silica gel accelerates this reaction, R_f = 0.24. ^{1}H NMR: δ 7.40−7.37 (m, 2 H), 7.26−7.24 (m, 3 H), 5.00 (s, 1 H), 3.27 (s, 3 H), 2.69 (s, 3 H), 1.55−1.47 (m, 1 H), 1.45 (d, J = 5.8 Hz, 1 H), 1.22 (d, J = 5.9 Hz, 1 H), 1.18−1.07 (m, 1 H), 1.00−0.82 (m, 2 H). ^{13}C NMR: δ 166.2 (s), 133.9 (s), 128.5 (d), 127.9 (d), 128.0 (d), 87.8 (d), 82.8 (s), 71.3 (s), 52.4 (q), 43.8 (q), 21.5 (t), 17.3 (s), 5.4 (t), 4.5 (t). IR ($CHCl_3$): 3004, 2850, 1741, 1435 cm^{-1}. MS: *m*/*z* (rel intensity) 309 (M^+, 4), 307 (M^+, 9), 272 (6), 240 (8), 190 (13), 158 (21), 135 (30), 120 (44), 118 (100), 91 (18), 77 (22), 59 (18), 54 (16).

1-(2-Chloroethyl)-2,3-dioxo-2,3,5,6-tetrahydropyrrolo-[1,2-*a*]isoquinoline (20).[15] A solution of cycloadduct **10** (30 mg, 0.10 mmol) in xylene (2.5 mL) was heated in a Sovirel tube at 150 °C for 3.5 h. Flash column chromatography (silica gel, eluent petroleum ether/ethyl acetate 2:1) of the reaction solution afforded product **20** (15 mg, 56%) as a solid, mp 123−125 °C (diethyl ether/petroleum ether), R_f = 0.36. ^{1}H NMR: δ 8.01 (d, J = 7.7 Hz, 1H), 7.61−7.44 (m, 2H), 7.39 (d, J = 7.3 Hz, 1H), 3.82−3.71 (m, 4H), 3.06 (t, J = 7.0 Hz, 4H). ^{13}C NMR: δ 185.0 (s), 158.6 (s), 157.2 (s), 137.8 (s), 133.1 (d), 129.5 (d), 129.4 (d), 127.9 (d), 125.1 (s), 104.9 (s), 42.1 (t), 36.2 (t), 29.7 (t), 26.2 (t). IR (CH_2Cl_2): 3047, 2984, 2964, 1744, 1704, 1593, 1405 cm^{-1}. MS: *m*/*z* (rel intensity) 263 (M^+, 20), 261 (M^+, 62), 226 (29), 212 (100), 198 (19), 184 (65), 171 (36), 156 (58). HRMS: 261.0556.

1-(1-(Chloromethyl)cyclopropyl)-2,3-dioxo-5,6-dihydropyrrolo[1,2-*a*]isoquinoline (21) and Methyl 5′-Chloro-2′-oxo-3′-(3″,4″-dihydroquinolin-1″-yl)spiro[cyclopropane-1,4′-pentanoate] (22). A solution of cycloadduct **11** (65 mg, 0.20 mmol) in xylene (3 mL) was heated in a Sovirel tube at 150 °C for 3 h. Flash column chromatography (silica gel, eluent petroleum ether/CH_2Cl_2/EtOAc 5:5:1) of the reaction mixture afforded an unseparable mixture (36 mg, 56%) of products **21** and **22** in a ratio of 1:2.5 (according to ^{1}H NMR). The products **21** and **22** could, however, be separated by fractionated recrystallization from CH_2Cl_2/petroleum ether affording **22** as pale yellow crystals and **21** as a red powder.

21: Mp 184−187 °C, R_f = 0.40. ^{1}H NMR: δ 8.63 (d, J = 7.7 Hz, 1 H), 7.59−7.43 (m, 2 H), 7.34 (d, J = 7.3 Hz, 1 H), 3.90−3.63 (m, 4 H), 3.04 (t, J = 6.2 Hz, 2 H), 1.13−1.02 (m, 2 H), 0.85−0.73 (m, 2 H). ^{13}C NMR: δ 185.7 (s), 159.6 (s), 156.9 (s), 137.6 (s), 133.2 (d), 131.3 (d), 128.9 (d), 127.2 (d), 124.3 (s), 108.4 (s), 53.2 (t), 36.3 (t), 29.2 (t), 17.0 (s), 15.7 (t, 2 C). IR (CH_2Cl_2): 2960, 2873, 1743, 1706, 1590, 1468 cm^{-1}. MS: *m*/*z* (rel intensity) 289 (M^+, 9), 287 (M^+, 29), 253 (24), 252 (100), 224 (42), 196 (36), 194 (27), 182 (26), 167 (37), 152 (29), 139 (41), 115 (38). HRMS: 287.0713.

22: Mp 138−141 °C, R_f = 0.40. ^{1}H NMR: δ 7.96 (dd, J = 7.7, 1.5 Hz, 1 H), 7.46 (td, J = 7.3, 1.5 Hz, 1 H), 7.32 (t, J = 7.7 Hz, 1 H), 7.21 (d, J = 7.4 Hz, 1 H), 4.00 (s, 1 H), 3.85 (t, J = 6.6 Hz, 2 H), 3.81 (s, 3 H), 3.78 and 3.65 (AB system, J = 11.7 Hz, 2 H), 3.11 (td, J = 7.0, 2.2 Hz, 2 H), 1.02−0.81 (m, 3 H), 0.78−0.69 (m, 1 H). ^{13}C NMR: δ 184.4 (s), 165.3 (s), 162.1 (s), 138.0 (s), 132.5 (d), 128.9 (s), 128.4 (d), 127.1 (d), 127.0 (d), 66.6 (d), 52.9 (q), 52.1 (t), 47.3 (t), 27.7 (t), 21.6 (s), 12.5 (t), 11.5 (t). IR (CH_2Cl_2): 3047, 2956, 1728, 1635, 1603, 1483 cm^{-1}, MS: *m*/*z* (rel intensity) 278 (14), 276 (40), 250 (36), 248 (100), 131 (37), 130 (59), 103 (42), 77 (24), 59 (33). Anal. Calcd for $C_{17}H_{18}ClNO_3$ (319.8): C, 63.85; H, 5.67; N, 4.38. Found: C, 63.50; H, 5.75; N, 4.10.

(1′*S,10b′*R**)-1′-Chloro-1′-(methoxycarbonyl)-6′,10b′-dihydrospiro[cyclopropane-1,2′-(5′*H*)-[2*H*]isoxazolo[2,3-*a*]-isoquinoline] (30).**[15] A solution of cycloadduct **10** (210 mg, 0.72 mmol) in toluene (6 mL) was heated in a Sovirel tube at 110 °C for 3 h. Flash column chromatography (Al_2O_3, eluent petroleum ether/CH_2Cl_2/ethyl acetate 5:5:1) gave 114 mg (54%) of cycloadduct **30** together with **10** (15 mg, 7%), mp 88−90 °C (CH_2Cl_2/petroleum ether), R_f = 0.61. ^{1}H NMR: δ 7.30−7.16 (m, 3 H), 7.07−7.03 (m, 1 H), 5.77 (s, 1 H), 3.92 (s, 3 H), 3.81 (td, J = 10.6; 4.7 Hz, 1 H), 3.31−3.22 (m, 1 H), 3.10 (dt, J = 11.0; 6.0 Hz, 1 H), 2.97−2.89 (m, 1 H)1.43−1.21 (m, 3 H), 1.19−0.87 (m, 1 H). ^{13}C NMR: δ 169.0 (s), 134.4 (s), 131.6 (s), 128.0 (d), 127.7 (d), 127.6 (d), 126.1 (d), 83.5 (s), 72.7 (s), 72.1 (d), 53.7 (q), 47.9 (t), 28.5 (t), 15.4 (t), 9.7 (t). IR (CH_2Cl_2): 3054, 2980, 1729, 1475, 1371 cm^{-1}. MS: *m*/*z* (rel intensity) 295 (M^+, 8), 293 (M^+, 25), 258 (12), 257 (30), 226 (27), 158 (97), 147 (54), 132 (84), 131 (97), 130 (100), 115 (83), 103 (79), 77 (75), 59 (99). Anal. Calcd for $C_{15}H_{16}ClNO_3$ (293.75): C, 61.33; H, 5.49; N, 4.77. Found: C, 61.10; H, 5.52; N, 4.39.

(1″*S,10b″*R**)-1″-Chloro-1′-(methoxycarbonyl)-6″,10″-dihydrodispiro[cyclopropane-1,1′-cyclopropane-2′,2″-(5″*H*)-[2*H*]isoxazolo[2,3-*a*]isoquinoline] (31).** A solution of **11** (200 mg, 0.62 mmol) in toluene (6 mL) was heated in a Sovirel tube at 110 °C for 3 h. Cycloadducts **11** (43 mg, 21%) and **31** (107 mg, 53%) were separated by flash column chromatography (Al_2O_3, eluent petroleum ether/CH_2Cl_2/EtOAc 5:5:1). Cycloadduct **31** is a solid consisting of an unseparable mixture of two diastereoisomers (1.8:1, according to ^{1}H NMR), R_f = 0.53. ^{1}H NMR: δ 7.28−7.13 (m, 3 H), 7.05−6.95 (m, 1 H), 5.82 (s, 1 H), 3.93 (s, 3 H), 4.05−3.80 (m, 1 H), 3.50−2.82 (m, 3 H), 1.71−1.47 (m, 2 H), 1.25 (d, J = 6.2 Hz, 1 H), 1.08−0.87 (m, 3 H); discernible signals for the minor diastereoisomer: 5.56 (s, 1 H), 3.87 (s, 3 H). ^{13}C NMR: (major diastereoisomer) δ 168.6 (s), 134.9 (s), 131.3 (s), 127.9 (d), 127.5 (d, 2C), 127.4 (d), 126.1 (d), 81.7 (s), 75.1 (s), 73.1 (d), 53.6 (q), 48.6 (t), 28.5 (t), 20.1 (t), 14.0 (s), 7.1 (t), 5.1 (t); (discernible signals of the minor diastereoisomer) δ 134.3 (s), 128.0 (d), 127.6 (d, 2C), 126.0 (d), 80.1 (s), 73.4 (s), 71.7 (d), 53.2 (q), 47.9 (t), 27.9 (t), 19.8 (t), 6.0 (t), 4.8 (t). IR: (CH_2Cl_2) 3045, 2977, 2956, 1736, 1433 cm^{-1}. MS: *m*/*z* (rel intensity) 284 (2), 147 (45), 130 (78), 115 (37), 84 (100), 59 (54), 54 (66). HRMS: 319.0975.

1-(Methoxycarbonyl)-4-oxo-3,4,6,7-tetrahydro-2*H*-benzo[*a*]quinolizine (32). A solution of cycloadduct **10** (162 mg, 0.55 mmol) in DMSO (4 mL) was heated in a Sovirel tube at 150 °C for 3 h. The DMSO was distilled off at 12 mmHg by heating in an oil bath at 100 °C. The crude product was purified by flash column chromatography (silica gel, eluent diethyl ether/petroleum ether 1:1) to afford an unseparable mixture of **32** and **20** in a ratio of 2:1 [32 mg, **32** (15%) and **20** (8%), according to ^{1}H NMR], R_f = 0.10. ^{1}H NMR: δ 7.38−7.28 (m, 2 H), 7.25−7.17 (m, 2 H), 3.74 (t, J = 6.2 Hz, 2 H), 3.59 (s, 3 H), 2.87 (t, J = 6.2 Hz, 2 H), 2.81−2.71 (m, 2 H), 2.69−2.57 (m, 2 H). ^{13}C NMR: δ 170.0 (s), 169.0 (s), 142.5 (s), 137.0 (s), 130.3 (s), 129.8 (d), 129.4 (d), 126.8 (d), 125.8 (d), 109.0 (s), 51.6 (q), 39.7 (t), 30.7 (t), 28.7 (t), 21.8 (t). MS: *m*/*z* (rel intensity) 257 (M$^+$, 14), 226 (7), 198 (45), 128 (43), 59 (69), 51 (100).

1′-(Methoxycarbonyl)-4′-oxo-3′,4′,6′,7′-tetrahydro-2′*H*-spiro[cyclopropane-1,3′-benzo[*a*]quinolizine] (33). A solution of cycloadduct **11** (263 mg, 0.82 mmol) in DMSO (6 mL) was heated in a Sovirel tube at 150 °C for 3 h. The DMSO was distilled off at 12 mmHg by heating in an oil bath at 100 °C. The crude material was purified by flash column chromatography (silica gel, eluent diethyl ether/petroleum ether 1:1) to afford **33** (49 mg, 21%), R_f = 0.39. ^{1}H NMR: δ 7.41−7.30 (m, 2 H), 7.24−7.17 (m, 2 H), 3.72 (t, J = 5.8 Hz, 2 H), 3.60 (s, 3 H), 2.89 (t, J = 5.8 Hz, 2 H), 2.65 (s, 2 H), 1.33−1.28 (m, 2 H), 0.82−0.76 (m, 2 H). ^{13}C NMR: δ 172.7 (s), 169.1 (s), 141.9 (s), 137.3 (s), 130.3 (s), 129.8 (d), 129.6 (d), 126.8 (d), 125.7 (d), 107.1 (s), 51.6 (q), 40.7 (t), 31.4 (t), 29.0 (t), 19.5 (s), 15.2 (t, 2 C). IR ($CHCl_3$): 2952, 1700, 1664, 1432, 1380 cm^{-1}. MS: *m*/*z* (rel intensity) 283 (M$^+$, 6), 282 (12), 268 (14), 224 (14), 115 (27), 77 (76), 59 (100). Anal. Calcd for $C_{17}H_{17}NO_3$ (283.3): C, 72.07; H, 6.05; N, 4.94. Found: C, 71.94; H, 6.15; N, 4.84.

8-(Methoxycarbonyl)-5-oxo-2,3,6,7-tetrahydro-1*H*-indolizine (34).[12] A solution of cycloadduct **13** (125 mg, 0.54 mmol) in DMSO (6 mL) was heated in a Sovirel tube at 100 °C for 5 h. The reaction mixture was poured into water (20 mL) and extracted three times with diethyl ether (20 mL). The combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. Flash column chromatography (silica gel, eluent diethyl ether) afforded **34** (87 mg, 83%) as a colorless solid, mp 70−71 °C (diisopropyl ether), R_f = 0.34. ^{1}H NMR: δ 3.67 (s, 3 H), 3.66 (t, J = 7.9 Hz, 2 H), 3.08 (tt, J = 7.9, 1.8 Hz, 2 H), 2.64−2.54 (m, 2 H), 2.50−2.41 (m, 2 H), 1.92 (quint, J = 7.8 Hz, 2 H). ^{13}C NMR: δ 169.8 (s), 167.8 (s), 153.7 (s), 100.9 (s), 51.6 (q), 46.3 (t), 32.1 (t), 31.2 (t), 21.7 (t), 21.5 (t). IR ($CDCl_3$): 2989, 2902, 1680, 1645, 1437, 1333 cm^{-1}. MS: *m*/*z* (rel intensity) 195 (M$^+$, 70), 180 (65), 164 (59), 136 (100), 108 (30), 106 (35), 80 (33), 41 (50). Anal. Calcd for $C_{10}H_{13}NO_3$ (195.2): C, 61.53; H, 6.71; N, 7.17. Found: C, 61.65; H, 6.84; N, 6.88.

8′-(Methoxycarbonyl)-5′-oxo-2′,3′,6′,7′-tetrahydro-1*H*-spiro[cyclopropane-1,6′-indolizine] (35). A solution of cycloadduct **14** (75 mg, 0.29 mmol) in DMSO (2 mL) was heated in a Sovirel tube at 100 °C for 3 h. The reaction mixture was poured into 10 mL of water and extracted three times with 15 mL of diethyl ether. Organic phases were dried over Na_2SO_4 and concentrated in vacuo. Flash column chromatography (silica gel, eluent diethyl ether) afforded **35** (47 mg, 73%) as a solid, mp 72−74 °C (diisopropyl ether), R_f = 0.54. ^{1}H NMR: δ 3.64 (s, 3 H), 3.63 (t, J = 7.3 Hz, 2 H), 3.10 (tt, J = 7.6, 1.8 Hz, 2 H), 2.48 (t, J = 1.8 Hz, 2 H), 1.93 (p, J = 7.3 Hz, 2 H), 1.21−1.20 (m, 2 H), 0.68−0.63 (m, 2 H). ^{13}C NMR: δ 172.3 (s), 167.5 (s), 153.3 (s), 98.6 (s), 51.1 (q), 46.4 (t), 31.8 (t), 30.8 (t), 21.4 (t), 19.9 (s), 16.4 (t, 2C). IR ($CDCl_3$): 2991, 2894, 1660, 1644, 1437, 1381 cm^{-1}. MS: *m*/*z* (rel intensity) 221 (M$^+$, 17), 206 (98), 162 (100), 134 (23), 106 (23), 77 (30), 65 (36), 53 (30), 41 (47). Anal. Calcd for $C_{12}H_{15}NO_3$ (221.25): C, 65.13; H, 6.84; N, 6.33. Found: C, 65.42; H, 6.88; N, 6.08.

Methyl 3-Chloro-1-aza-2-oxatricyclo[5.3.0.0^{3,6}]decane-6-carboxylate (38). A solution of **13** (100 mg, 0.43 mmol) and 400 mg of Al_2O_3, (activity I, pH 7.00 ± 0.05, Fluka) in 4 mL of CH_2Cl_2 was stirred at room temperature for 3 d. The reaction mixture was filtered and concentrated in vacuo to give 97 mg of a mixture of **38** and **13** (6:1) as a yellow oil, R_f = 0.23 (diethyl ether/petroleum ether 1:1). ^{1}H NMR: δ 4.47 (t, J = 4.0 Hz, 1 H), 3.78 (s, 3 H), 3.59−3.46 (m, 1 H), 2.93−2.69 (m, 1 H), 2.67−2.32 (m, 3 H), 1.96−1.64 (m, 5 H). ^{13}C NMR: δ 169.9 (s), 102.1 (s), 72.9 (s), 70.3 (d), 56.8 (q), 52.9 (t), 33.2 (t), 27.7 (t), 25.8 (t), 22.0 (t). IR ($CDCl_3$): 2957, 1726, 1436 cm^{-1}. MS: *m*/*z* (rel intensity) 233 (M$^+$, 2), 231 (M$^+$, 5), 195 (70), 180 (60), 164 (56), 136 (94), 122 (100), 94 (52), 86 (64), 67 (57), 55 (71).

Methyl Spiro[cyclopropane-1,4′-(3′-chloro-1′-aza-2′-oxatricyclo[5.3.0.0^{3,6}]decane-6′-carboxylate)] (15). A solution of the mixture 5:1 of **14** and **15** (101 mg, 0.39 mmol) and 400 mg of Al_2O_3 (activity I, pH 7.00 ± 0.05, Fluka) in CH_2Cl_2 (4 mL) was stirred at room temperature for 4 h. The reaction mixture was filtered and concentrated in vacuo to give 95 mg of **15** (94%), R_f = 0.22 (diethyl ether/petroleum ether 1:1). ^{1}H NMR: δ 4.46 (t, J = 7.0 Hz, 1 H), 3.80 (s, 3 H), 3.63−3.46 (m, 1 H), 3.04−2.87 (m, 1 H), 2.69 and 2.21 (AB system, J = 11.3 Hz, 2 H), 2.11−1.93 (m, 1 H), 1.91−1.70 (m, 3 H), 1.04−0.88 (m, 1 H), 0.86−0.72 (m, 2 H), 0.55−0.47 (m, 1 H). ^{13}C NMR: δ 169.9 (s), 107.5 (s), 71.2 (d), 70.4 (s), 56.5 (t), 52.8 (q), 30.0 (t), 28.4 (s), 27.4 (t), 25.5 (t), 12.4 (t), 8.0 (t). IR ($CDCl_3$): 2957, 1728, 1437 cm^{-1}. MS: *m*/*z* (rel intensity) 259 (M$^+$, 2), 257 (M$^+$, 7), 221 (15), 206 (67), 190 (17), 162 (84), 154 (45), 86 (100), 59 (23), 55 (42), 53 (40).

(1*S,4*S**,5*S**)-1-Chloro-3-methyl-5-(methoxycarbonyl)-4-phenyl-3-aza-2-oxabicyclo[3.2.0]heptane (39).**[15] A solution of cycloadduct **17** (200 mg, 0.71 mmol) in DMSO (6 mL) was heated in a Sovirel tube at 100 °C for 7 h. Flash column chromatography (silica gel, eluent petroleum ether/ethyl acetate 5:1) afforded **39** (164 mg, 82%) as a solid, mp 68−70 °C (diisopropyl ether), R_f = 0.5. ^{1}H NMR: δ 7.35−7.32 (m, 5 H), 4.47 (s, 1 H), 3.87 (s, 3 H), 2.85 (s, 3 H), 2.92−2.60 (m, 2 H), 2.32 (ddd, J = 12.1, 10.9, 6.2 Hz, 1 H), 2.03 (ddd, J = 12.1, 10.2, 7.3 Hz, 1 H). ^{13}C NMR: δ 169.3 (s), 133.8 (s), 129.5 (d), 128.5 (d), 128.1 (d), 128.0 (d), 127.7 (d), 99.1 (s), 74.6 (d), 71.1 (s), 52.6 (q), 43.7 (q), 37.6 (t), 16.3 (t). IR (CH_2Cl_2): 2957, 2883, 1729, 1437 cm^{-1}. MS: *m*/*z* (rel intensity) 283 (M$^+$, 3), 281 (M$^+$, 8), 204 (98), 172 (73), 144 (50), 134 (73), 118 (100). Anal. Calcd for $C_{14}H_{16}ClNO_3$ (281.7): C, 59.68; H, 5.72; N, 4.97. Found: C, 59.60; H, 5.80; N, 5.20.

(1′*S,4′*S**,5′*S**)-1′-Chloro-3′-methyl-5′-(methoxycarbonyl)-4′-phenylspiro[1,7′-cyclopropane-3′-aza-2′-oxabicyclo-[3.2.0]heptane] (40).** A solution of the cycloadduct **19** (145 mg, 0.47 mmol) in DMSO (4 mL) was heated at 100 °C for 2 h. The reaction mixture was poured into 30 mL of water and extracted three times with 30 mL of diethyl ether. Organic phases were dried over Na_2SO_4 and concentrated in vacuo. Flash column chromatography (silica gel, eluent diethyl ether/petroleum ether 1:6) of the residue afforded **40** (119 mg, 82%) as an oil, R_f = 0.36. ^{1}H NMR: δ 7.38−7.32 (m, 5 H), 4.52 (s, 1 H), 3.89 (s, 3 H), 2.84 (s, 3 H), 2.51 and 2.17 (AB system, J = 12.1 Hz, 2 H), 1.16−1.98 (m, 2 H), 0.8−0.73 (m, 2 H). ^{13}C NMR: δ 169.5 (s), 134.2 (s), 128.6 (d), 128.1 (d), 127.9 (d), 104.7 (s), 74.6 (d), 69.1 (s), 52.6 (q), 43.5 (q), 30.2 (s), 26.4 (t), 14.4

(t), 10.7 (t). IR ($CHCl_3$): 3002, 2956, 2880, 1727, 1434, 1356 cm^{-1}. MS: *m*/*z* (rel intensity) 309 (M^+, 1), 307 (M^+, 3), 256 (9), 204 (34), 172 (14), 134 (100), 118 (54), 91 (26), 77 (52), 42 (76). Anal. Calcd for $C_{16}H_{18}ClNO_3$ (307.8): C, 62.44; H, 5.89; N, 4.55. Found C, 62.28; H, 6.00; N, 4.46.

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Supporting Information Available: Tables of crystal data and structure refinement, atomic and hydrogen coordinates, isotropic and anisotropic displacement parameters, bond lengths and angles in the crystals of compounds **10**, **20**, **30**, and **39** (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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