Reaction of difluorocarbene with 2*H*-azirines: generation and transformations of strained azomethine ylides — aziriniodifluoromethanides*,**

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The reaction of difluorocarbene with azirines affords a new type of azomethine ylides, *viz.*, strained aziriniodifluoromethanides. 1,3-Dipolar cycloadditions of ylides derived from 2-unsubstituted 3-arylazirines to dimethyl acetylenedicarboxylate and aldehydes give derivatives of 2,2-difluoro-1-azabicyclo[3.1.0]hex-3-ene-3,4-dicarboxylic acids and 1,4-oxazin-3(4*H*)-ones, respectively. Ylides derived from 2-mono- and 2,2-disubstituted azirines undergo isomerization to 2-aza-1,3-diene derivatives. 2,2-Difluoro-1-azabicyclo[3.1.0]hex-3-enes are transformed into 2-fluoropyridine derivatives in high yields and react with amines to give 2,4-diamino-1-azabicyclo[3.1.0]hex-2-ene derivatives.

Key words: azirines, difluorocarbene, azomethine ylides, cycloaddition, fluoro-substituted heterocycles.

Chemistry of 2*H*-azirine derivatives has been extensively studied over the last decades. 2*H*-Azirine is the smallest heterocyclic system containing one N atom and a double bond, which is highly strained and, consequently, highly reactive. The reactions of azirines with various electrophilic and nucleophilic reagents were investigated.[2,3] The concerted reactions of azirines with dipoles and dienes were also examined.[4] However, the reactions of azirines with carbenes, which could afford unusual strained azomethine ylides, remain virtually unknown. In the only study on reactions of dichlorocarbene, which was generated by thermal decomposition of phenyl(trichloromethyl)mercury, with azirines, *N*-(dichlorovinyl)-*N*-vinylamines were prepared in low yields.[5] Two possible pathways of their formation were proposed, *viz.*, *via* the corresponding 1-azabicyclobutane formed upon the addition of dichlorocarbene to azirine or *via* azirinium ylide formed as a result of the attack of dichlorocarbene on the lone electron pair of the N atom of azirine. However, no attempts were made to prove the formation of the ylide intermediate.

Earlier, we have demonstrated that it is not always possible to trap dichloro-substituted azomethine ylides by means of 1,3-dipolar cycloaddition because these compounds give 1,3-cyclization products, *i.e.*, the corresponding dichloroaziridines, rather than 1,3-dipolar cycloaddition products to dipolarophiles.[6—9] Recently, it has been found that difluoro-substituted azomethine ylides are readily involved in cycloaddition and do not give cyclization products.[10—13] This gives promise that fluoro-substituted azirinium ylides may be prepared by 1,3-dipolar cycloaddition. In the present study, we developed a procedure for the generation of difluoro-substituted azirinium ylides, studied chemical transformations of ylides containing the differently substituted azirine ring, and investigated the chemical behavior of their primary reaction products.

We found that 3-aryl-2*H*-azirines **1** react with difluorocarbene to form unstable intermediates, *viz.*, difluoro-substituted azirinium ylides **2** (Scheme 1), which can be isolated as cycloadducts with active dipolarophiles. In some cases, primary adducts of 1,3-dipolar cycloaddition are unstable and undergo further transformations in the course of the reaction or in the step of isolation. Difluorocarbene was generated by reduction of CF_2Br_2 with lead in the presence of Bu_4NBr in dichloromethane. The structures of the products were established according to standard procedures by ^1H and ^{13}C NMR and IR spectroscopy. Their compositions were confirmed by elemental analysis.

The reactions of azirines **1a—e** with difluorocarbene in the presence of dimethyl acetylenedicarboxylate (DMAD) as a dipolarophile yielded dimethyl 5-aryl-2,2-difluoro-1-azabicyclo[3.1.0]hex-3-ene-3,4-dicarboxy-

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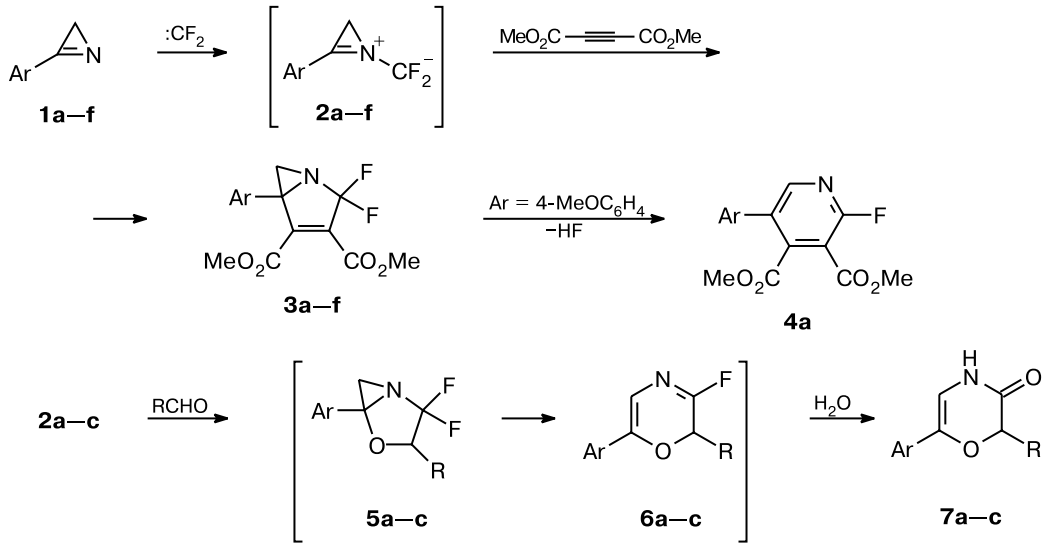
Scheme 1



1—3	Ar	1—3	Ar	5—7	Ar	R
a	Ph	**d**	4-BrC_6H_4	**a**	Ph	Ph
b	4-MeC_6H_4	**e**	2,4-$Cl_2C_6H_3$	**b**	4-BrC_6H_4	Ph
c	4-ClC_6H_4	**f**	4-$MeOC_6H_4$	**c**	4-BrC_6H_4	Me

lates **3a—e**. It should be noted that primary cycloaddition products of difluoro-substituted azomethine ylides to C=C- and C≡C-dipolarophiles containing the difluoromethylene group at the N atom are generally unstable. Under the reaction conditions, these compounds readily undergo dehydrofluorination to give fluoropyrrole derivatives or are hydrolyzed to the corresponding lactams in the course of chromatographic isolation.[11—14] Compounds **3a—e** are rather stable. They withstand chromatography on SiO_2 and can be stored without decomposition at −20 °C over a long period. Higher stability of compounds **3a—e** compared to their monocyclic analogs is apparently associated with their high resistance to nucleophilic substitution of fluorine atoms due to rigidity of the azabicyclo[3.1.0]hex-3-ene skeleton. However, fluoropyridine **4a** resulted from ring expansion and dehydrofluorination of primary cycloadduct **3f** was isolated upon the reaction of azirine **1f** with difluorocarbene in the presence of DMAD. This is apparently associated with the fact that the electron-donating substituents in the aryl moiety accelerate transformations of arylfluoropyrrole derivatives.[14]

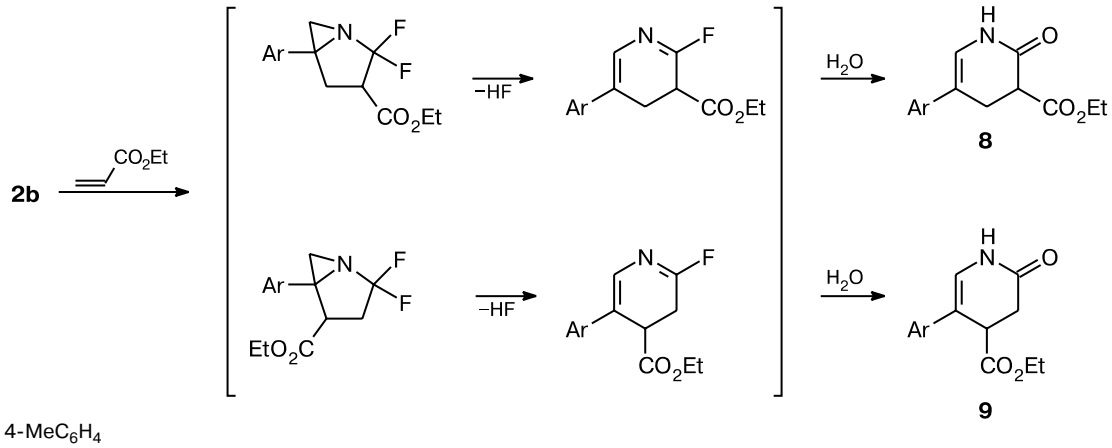
In the reactions of ylides **2a—c** with aldehydes as dipolarophiles, primary 2,2-difluoro-4-oxa-1-azabicyclo[3.1.0]hexanes **5a—c** were not isolated because they readily underwent ring expansion to 3-fluoro-1,4-oxazine derivatives **6a—c**. The latter were hydrolyzed in the course of chromatographic isolation to give 1,4-oxazin-3(4*H*)-one derivatives **7a—c**.

The reactions of azirinium ylides with less reactive dipolarophiles produce cycloaddition products in low yields. Unlike the reactions with aldehydes, the reaction of ylide **2b** with ethyl acrylate proceeds not only in low yield but also with low regioselectivity to give ethyl 2-oxo-1,2,3,4-tetrahydropyridine-3-carboxylate **8** (4%) and ethyl 2-oxo-1,2,3,4-tetrahydropyridine-4-carboxylate **9** (8%) (Scheme 2).

The structures of the isomers were established based on analysis of the ^{1}H NMR and 2D NOESY spectra. The ^{1}H NMR spectrum of compound **8** shows a long-range spin coupling between the H(4) protons (δ 2.91 and 3.23, J = 1.2—1.4 Hz) and the H(6) proton (δ 6.45). The NOESY spectrum of compound **8** reveals cross-peaks between the *ortho*-protons of the aromatic ring (δ 7.23) and the H(4) protons (δ 2.91 and 3.23). The NOESY spectrum of compound **9** shows a cross-peak between the *ortho*-protons of the aromatic ring (δ 7.30) and the methine proton H(4) (δ 3.78).

The intramolecular cycloaddition of fluoro-substituted azomethine ylides occurs readily even with nonactivated C=C-dipolarophiles[15] and sometimes with poorly reactive dipolarophiles, such as the ester carbonyl group.[16] In this connection, it was of interest to study the reaction of difluorocarbene with azirine **10** containing the incorporated dipolarophilic fragment. However, we isolated not the expected product of intramolecular cycloaddition of azirinium ylide **11** to the internal dipolarophile but isocyanate **12** (Scheme 3). The structure of the latter was established by spectroscopy and confirmed by its transformation into urea **13** upon treatment with morpholine. It should be noted that the reactions of difluorocarbene with

Scheme 2



8, 9: Ar = 4-MeC_6H_4

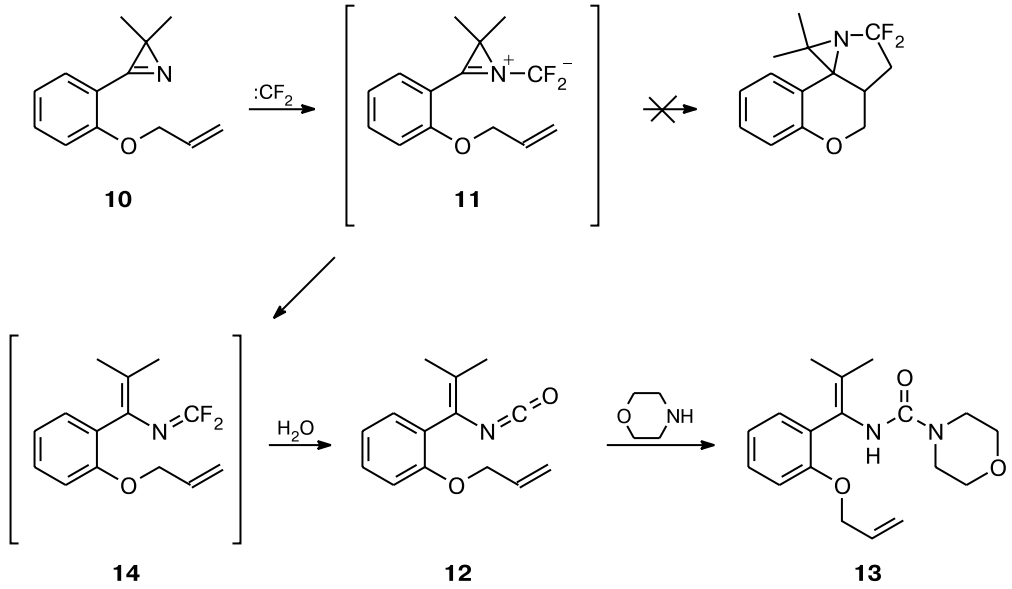
azirine **10** in the presence of DMAD did not yield cycloadducts either.

This result is apparently attributable to the fact that considerable steric crowding of azirinium ylide precludes its cycloaddition; instead, the ylide undergoes isomerization to azadiene **14**, which is hydrolyzed to give isocyanate **12** (see Scheme 3). It appeared that isomerization of azirinium ylides generated from difluorocarbene and 2-mono- or 2,2-disubstituted azirines is the major reaction pathway. For example, the reactions of azirines **15** and **16** with difluorocarbene afforded the corresponding isocyanates **17** and **18** (Scheme 4). The same products were isolated from the reaction in the presence of DMAD as a dipolarophile. The structure of isocyanate **17** was confirmed by its transformation into ureas **19a—e**.

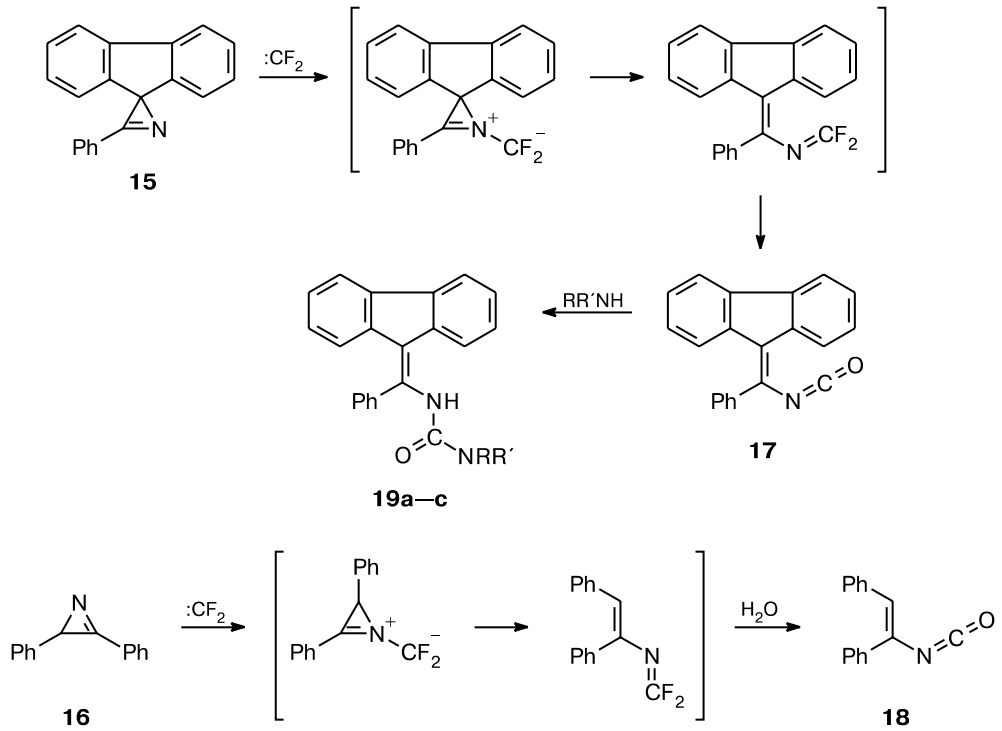
The spectroscopic characteristics of isocyanate **18** are identical with the published data for this compound prepared according to another procedure.[17] An attempt to perform heterocyclization involving the *N*-vinylisocyanate fragment of compound **17** upon the action of *N*-benzylidenebenzylamine failed because the latter is more rapidly transformed into *N*-benzylamine followed by its reaction with isocyanate **17** to form urea **19c**.

Presumably, low yields of the cycloadducts obtained in the reactions of azirines **1** with difluorocarbene in the presence of dipolarophiles, particularly, in the presence of poorly reactive dipolarophiles, are attributable to the competitive isomerization of azirinium ylides **2** to unstable *gem*-difluoroazadienes.

Scheme 3



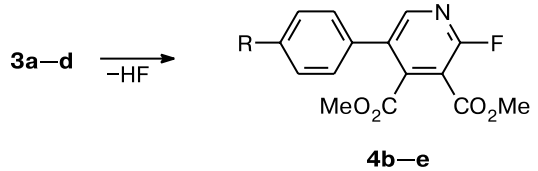
Scheme 4



19: R + R′ = —$(CH_2)_5$— (**a**), —$(CH_2)_2$—O—$(CH_2)_2$— (**b**);
R = Bn, R′ = H (**c**)

Since polyfunctional bicyclic compounds **3** contain the highly strained three-membered ring, the difluoromethylene group at the N atom, and other reactive functional groups, one would expect that these compounds could subject to various synthetically useful transformations. Actually, compounds **3** are stable in the crystalline state at low temperature but are smoothly transformed into 2-fluoropyridine derivatives **4** on storage of their solutions at ~20 °C (Scheme 5).

Scheme 5



4: R = H (**b**), 4-MeC_6H_4 (**c**), 4-ClC_6H_4 (**d**), 4-BrC_6H_4 (**e**)

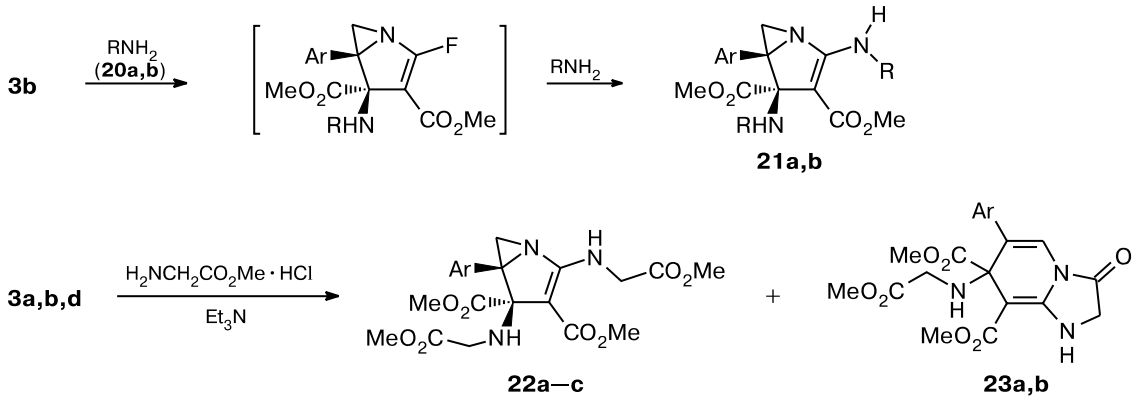
We also found that compounds **3** can be involved not only in ring expansion reactions (the strain energy of the three-membered ring is the driving force for this reaction) but also in reactions with retention of the azabicyclo[3.1.0]hexene skeleton. For example, the reaction of difluoride **3b** with amines **20a,b** afforded 1-azabicyclo[3.1.0]hex-2-ene derivatives **21a,b** (Scheme 6).

The stereochemistry of compounds **21a,b** was established by ^{1}H NMR spectroscopy and 2D NOESY experiments. It is known[8,18—21] that in the ^{1}H NMR spectra of tetrahydro- and 2,3-dihydropyrrole derivatives, the signals for the protons of the MeO_2C group at C(3), which is *cis*-oriented with respect to the aryl group at C(2), are shifted upfield ($\delta < 3.4$). The chemical shifts of the protons of the MeO_2C groups in compounds **21a,b** are larger than 3.65 ppm, which is indicative of the *trans* arrangement of the aryl and MeO_2C groups. In addition, the NOESY spectrum of compound **21b** shows a cross-peak between the protons of the aromatic ring at C(5) and the benzyl proton of the $PhCH_2N$ group at C(4) (δ 3.30).

The most probable mechanism of the formation of compounds **21** involves *tele*-substitution (S_N2'-reaction) of one F atom with amine followed by the replacement of the second F atom as a result of the following sequence of reactions: the addition of the amine and then dehydrofluorination.

The reaction of azirines **3a,b,d** with glycine methyl ester afforded 1-azabicyclo[3.1.0]hex-2-enes **22a—c** as the major products. In addition, the reactions of **3a,b** gave imidazo[1,2-*a*]pyridine derivatives **23a,b** in low yields. Although compounds **22** seem to be precursors of com-

Scheme 6



21: Ar = 4-MeC_6H_4; R = Me (**a**), $PhCH_2$ (**b**)
22, 23: Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-BrC_6H_4 (**c**)

pounds **23**, attempts to transform them into **23** failed under various reaction conditions. Apparently, the replacement of the second F atom followed by cyclization is preceded by ring expansion to form the 2-fluoropyridine derivative.

To summarize, we found that the reactions of difluorocarbene with azirines give a new type of azomethine ylides, *viz.*, strained azirinium difluoromethanides. Depending on the structure, the latter can be involved in 1,3-dipolar cycloaddition or undergo isomerization with the opening of the three-membered ring to give *gem*-difluoroazadienes. It was demonstrated that azirinium difluoromethanides can serve as synthetic equivalents of both $C^+—N—C^-$ and $C^+—C—N—C^-$ synthons in the carbene-ylide methodology of the synthesis of heterocycles containing unusual combinations of structural fragments.

Experimental

The IR spectra were recorded on a UR-20 spectrophotometer; the thickness of the absorbing layer was 400 μm. The NMR spectra were measured on a Bruker DPX-300 instrument (300 MHz for ^1H and 75 MHz for ^{13}C). Elemental analysis was carried out on an HP-185B C,H,N-analyzer. The course of the reactions was monitored by TLC on Silufol-254 plates. The reaction mixtures were separated by column chromatography on LS 5/40 silica gel (Chemapol).

3-Aryl-2*H*-azirines **1a—f**,[22] azirine **10**,[23] azirine **15**,[24] and azirine **16** [25] were prepared according to known procedures.

3-(2,4-Dichlorophenyl)-2*H*-azirine (1e). Sodium azide (9.15 g, 0.14 mol) was added to a stirred solution of 1-(1,2-dibromoethyl)-2,4-dichlorobenzene (30 g, 0.09 mol) in anhydrous DMSO (300 mL) at 15—20 °C for 45 min. The reaction mixture was stirred at 24—26 °C for 14 h and cooled to 12—14 °C. Then an aqueous NaOH solution (3.6 g, 0.09 mol in 4.0 mL of H_2O) was added dropwise. The reaction solution was stirred at 24—26 °C for 24 h and poured into 2% aqueous $NaHCO_3$ (400 mL). The organic layer was separated and the aqueous layer was extracted two times with CH_2Cl_2. The combined extracts were washed with water, dried with $MgSO_4$, and filtered through cotton. The dichloromethane was removed *in vacuo*. Hexane (40 mL) was added to the red oil containing 1-(1-azidovinyl)-2,4-dichlorobenzene. The solution was chromatographed on Al_2O_3 (40 g) using hexane (200 mL) as the eluent. The hexane was removed *in vacuo*, the residue was dissolved in toluene (250 mL), and the solution was refluxed for 1.5 h. Then the solvent was removed *in vacuo*. Azirine **1e** was isolated from the residue by sublimation (65—75 °C/1 Torr) in a yield of 9.39 g (56 %), m.p. 67 °C. Found (%): C, 51.62; H, 2.74; N, 7.42. $C_8H_5Cl_2N$. Calculated (%): C, 51.65; H, 2.71; N, 7.53. IR (CCl_4), ν/cm^{-1}: 1750 (C=N). ^1H NMR ($CDCl_3$), δ: 1.84 (s, 2 H, H(2)); 7.64 (d, 1 H, Ar, J = 8.3 Hz); 7.75 (dd, 1 H, Ar, J = 8.3 Hz, J = 1.8 Hz); 7.98 (d, 1 H, Ar, J = 1.8 Hz). ^{13}C NMR ($CDCl_3$), δ: 19.9 C(2); 125.0, 127.7, 130.7, 130.9, 133.3, 136.9 C(Ar); 164.4 C(3).

Reaction of azirines 1 with difluorocarbene in the presence of dimethyl acetylenedicarboxylate (DMAD) or aldehydes (general procedure). ***A.*** Tetrabutylammonium bromide (3.14 g, 11.8 mmol), azirine (5 mmol), DMAD (2.13 g, 15 mmol) or aldehyde (15—30 mmol), and CF_2Br_2 (1.12 mL, 12.3 mmol) were added to a flask containing freshly prepared activated lead[12] (1.91 g, 9.23 mmol) under a layer of CH_2Cl_2 (20 mL). The flask was closed with a stopper to withstand moderate excessive pressure. The reaction mixture was stirred with a magnetic stirrer at 40—45 °C or sonicated at the same temperature until the lead completely consumed. The solvent was removed under reduced pressure and the products were isolated by column chromatography on silica gel.

Dimethyl 2,2-difluoro-5-phenyl-1-azabicyclo[3.1.0]hex-3-ene-3,4-dicarboxylate (3a). Compound **3a** was prepared from azirine **1a** (1 g, 8.55 mmol) and DMAD (40—45 °C, 3 h) in a yield of 1.07 g (41%); chromatography was performed with an 8 : 1 hexane—AcOEt mixture as the eluent. The physicochemical constants and spectroscopic characteristics of compound **3a** coincided with those published earlier.[1]

Dimethyl 2,2-difluoro-5-(4-tolyl)-1-azabicyclo[3.1.0]hex-3-ene-3,4-dicarboxylate (3b). Compound **3b** was prepared from

azirine **1b** (1 g, 7.63 mmol) and DMAD (3.5 h, sonication). After chromatography, the yield was 1.06 g (43%), m.p. 71—73 °C (from diethyl ether—pentane). Found (%): C, 59.42; H, 4.56; N, 4.36. $C_{16}H_{15}F_2NO_4$. Calculated (%): C, 59.44; H, 4.68; N, 4.33. IR (CCl_4), ν/cm^{-1}: 1755, 1660 (C=O/C=C). ^{1}H NMR ($CDCl_3$), δ: 2.36 (s, 3 H, Me); 2.67 (d, 1 H, H(6), $^4J_{H,F}$ = 2.6 Hz); 2.83 (d, 1 H, H(6), $^4J_{H,F}$ = 0.9 Hz); 3.77 and 3.85 (both s, 3 H each, MeO); 7.18 and 7.28 (both d, 2 H each, Ar, J = 7.9 Hz). ^{13}C NMR ($CDCl_3$), δ: 20.9 (s, Me); 49.2 (dd, C(6), $^3J_{C,F}$ = 2.8 Hz, $^3J_{C,F}$ = 4.4 Hz); 52.3 and 52.6 (both MeO); 55.0 (dd, C(5), $^3J_{C,F}$ = 2.2 Hz, $^3J_{C,F}$ = 3.3 Hz); 123.9 (dd, C(3), $^2J_{C,F}$ = 30.0 Hz, $^2J_{C,F}$ = 38.0 Hz); 127.8, 129.2, 138.9 (Ar); 128.1 (d, Ar, $^4J_{C,F}$ = 4.4 Hz); 129.2 (dd, C(2), $^1J_{C,F}$ = 244.0 Hz, $^1J_{C,F}$ = 254.0 Hz); 155.0 (t, C(4), $^3J_{C,F}$ = 5.0 Hz); 159.7 (t, C=O, $^3J_{C,F}$ = 2.8 Hz); 162.3 (s, C=O).

Dimethyl 5-(4-chlorophenyl)-2,2-difluoro-1-azabicyclo[3.1.0]hex-3-ene-3,4-dicarboxylate (3c). Compound **3c** was prepared from azirine **1c** (1 g, 6.60 mmol) and DMAD (3.5 h, sonication). After chromatography, the yield was 0.77 g (36%), m.p. 73 °C (from diethyl ether—hexane). Found (%): C, 52.43; H, 3.63; N, 3.87. $C_{15}H_{12}ClF_2NO_4$. Calculated (%): C, 52.42; H, 3.52; N, 4.08. IR (CCl_4), ν/cm^{-1}: 1750, 1660 (C=O/C=C). ^{1}H NMR ($CDCl_3$), δ: 2.67 (d, 1 H, H(6), $^4J_{H,F}$ = 2.2 Hz); 2.79 (s, 1 H, H(6)); 3.75 and 3.83 (both s, 3 H each, MeO); 7.33 (m, 4 H, Ar). ^{13}C NMR ($CDCl_3$), δ: 49.2 (dd, C(6), $^3J_{C,F}$ = 2.7 Hz, $^3J_{C,F}$ = 4.4 Hz); 52.3 and 52.6 (both MeO); 54.3 (dd, C(5), $^3J_{C,F}$ = 4.0 Hz, $^3J_{C,F}$ = 2.0 Hz); 124.4 (dd, C(3), $^2J_{C,F}$ = 30.0 Hz, $^2J_{C,F}$ = 38.0 Hz); 128.7, 129.3, 135.0 (Ar); 129.8, (d, Ar, $^4J_{C,F}$ = 5.0 Hz); 129.0 (dd, C(2), $^1J_{C,F}$ = 245.0 Hz, $^1J_{C,F}$ = 255.0 Hz); 153.9 (t, C(4), $^3J_{C,F}$ = 5.0 Hz); 159.5 (t, C=O, $^3J_{C,F}$ = 2.8 Hz); 162.3 (C=O).

Dimethyl 5-(4-bromophenyl)-2,2-difluoro-1-azabicyclo[3.1.0]hex-3-ene-3,4-dicarboxylate (3d). Compound **3d** was prepared from azirine **1d** (1 g, 5.10 mmol) and DMAD (40—45 °C, 4.5 h). After chromatography, the yield was 0.673 g (34%), m.p. 74—76 °C (from diethyl ether—pentane). Found (%): C, 46.41; H, 3.26; N, 3.73. $C_{15}H_{12}BrF_2NO_4$. Calculated (%): C, 46.41; H, 3.12; N, 3.61. IR (CCl_4), ν/cm^{-1}: 1755, 1655 (C=O/C=C). ^{1}H NMR ($CDCl_3$), δ: 2.69 (d, 1 H, H(6), $^4J_{H,F}$ = 2.2 Hz); 2.79 (s, 1 H, H(6)); 3.78 and 3.85 (both s, 3 H each, MeO); 7.28 and 7.51 (both d, 2 H each, Ar, J = 8.4 Hz). ^{13}C NMR ($CDCl_3$), δ: 50.0 (dd, C(6), $^3J_{C,F}$ = 2.8 Hz, $^3J_{C,F}$ = 5.4 Hz); 53.2 and 53.5 (both MeO); 55.0 (dd, C(5), $^3J_{C,F}$ = 2.5 Hz, $^3J_{C,F}$ = 3.5 Hz); 124.6 (dd, C(3), $^2J_{C,F}$ = 30.0 Hz, $^2J_{C,F}$ = 38.0 Hz); 123.8, 129.6, 131.7 (Ar); 129.0 (dd, C(2), $^1J_{C,F}$ = 245.0 Hz, $^1J_{C,F}$ = 255.0 Hz); 129.8 (d, Ar, $^4J_{C,F}$ = 5.0 Hz); 153.9 (t, C(4), $^3J_{C,F}$ = 4.7 Hz); 160.2 (t, C=O, $^3J_{C,F}$ = 2.3 Hz); 162.3 (C=O).

Dimethyl 5-(2,4-dichlorophenyl)-2,2-difluoro-1-azabicyclo[3.1.0]hex-3-ene-3,4-dicarboxylate (3e). Compound **3e** was prepared from azirine **1e** (0.83 g, 4.46 mmol) and DMAD (7 h, sonication). After chromatography, the yield was 0.490 g (29%), m.p. 72—74 °C (from diethyl ether—pentane). Found (%): C, 47.64; H, 2.98; N, 3.54. $C_{15}H_{11}Cl_2F_2NO_4$. Calculated (%): C, 47.64; H, 2.93; N, 3.70. IR (CCl_4), ν/cm^{-1}: 1750, 1660 (C=O/C=C). ^{1}H NMR ($CDCl_3$), δ: 2.69 (d, 1 H, H(6), $^4J_{H,F}$ = 2.6 Hz); 2.80 (d, 1 H, H(6), $^4J_{H,F}$ = 0.8 Hz); 3.80 and 3.85 (both s, 3 H each, MeO); 7.25 (dd, 1 H, Ar, J = 8.4 Hz, J = 2.1 Hz); 7.45 (d, 1 H, Ar, J = 8.4 Hz); 7.50 (d, 1 H, Ar, J = 2.1 Hz). ^{13}C NMR ($CDCl_3$), δ: 49.3 (dd, C(6), $^3J_{C,F}$ = 2.3 Hz, $^3J_{C,F}$ = 6.9 Hz); 52.5 and 52.8 (both MeO); 53.7 (dd, C(5), $^3J_{C,F}$ = 2.3 Hz, $^3J_{C,F}$ = 3.5 Hz); 125.5 (dd, C(3), $^2J_{C,F}$ = 30.0 Hz, $^2J_{C,F}$ = 38.0 Hz); 128.9 (dd, C(2), $^1J_{C,F}$ = 246.0 Hz, $^1J_{C,F}$ = 255.0 Hz); 127.3, 130.0, 130.5 132.8, 133.5 (Ar); 131.6 (d, Ar, $^4J_{C,F}$ = 4.6 Hz); 153.0 (t, C(4), $^3J_{C,F}$ = 4.0 Hz); 159.5 (t, C=O, $^3J_{C,F}$ = 2.9 Hz); 161.9 (C=O).

2,6-Diphenyl-2*H*-1,4-oxazin-3(4*H*)-one (7a). Compound **7a** was prepared from azirine **1a** (1 g, 8.55 mmol) and benzaldehyde (4 h, sonication) in a yield of 0.901 g (42%). The physicochemical constants and spectroscopic characteristics of compound **7a** coincided with those published earlier.[1]

6-(4-Bromophenyl)-2-phenyl-2*H*-1,4-oxazin-3(4*H*)-one (7b). Compound **7b** was prepared from azirine **1d** (1 g, 5.1 mmol) and benzaldehyde (5 h, sonication) (0.438 g, 26%), m.p. 179—181 °C (from $CHCl_3$—diethyl ether). Found (%): C, 58.38; H, 3.68; N, 3.98. $C_{16}H_{12}BrNO_2$. Calculated (%): C, 58.20; H, 3.66; N, 4.24. IR ($CHCl_3$), ν/cm^{-1}: 3410, 3210 (NH); 1705 (C=O). ^{1}H NMR (DMSO-d_6), δ: 5.64 (s, 1 H, H(2)); 6.69 (d, 1 H, H(5), J = 4.8 Hz); 7.34—7.50 (m, 9 H, Ar); 10.14 (d, 1 H, NH, J = 4.8 Hz). ^{13}C NMR (DMSO-d_6), δ: 78.2 (C(2)); 105.6 (C(5)); 121.1, 125.7, 127.7, 129.4, 129.6, 132.2, 132.7 (Ar); 135.9, 136.4 (Ar/C(6)); 164.8 (C=O).

6-(4-Bromophenyl)-2-methyl-2*H*-1,4-oxazin-3(4*H*)-one (7c). Compound **7c** was prepared from azirine **1d** (1 g, 5.1 mmol) and acetaldehyde (6 h, sonication) in a yield of 0.242 g (18%), m.p. 194—196 °C (from CH_2Cl_2—diethyl ether). Found (%): C, 49.52; H, 3.76; N, 4.91. $C_{11}H_{10}BrNO_2$. Calculated (%): C, 49.28; H, 3.76; N, 5.22. IR ($CHCl_3$), ν/cm^{-1}: 3415, 3215 (NH); 1705 (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.61 (d, 3 H, Me, J = 6.7 Hz); 4.62 (q, 1 H, H(2), J = 6.7 Hz); 6.31 (d, 1 H, H(5), J = 4.2 Hz); 7.36 and 7.49 (both d, 2 H each, Ar, J = 8.4 Hz); 7.57 (br.s, 1 H, NH). ^{13}C NMR (DMSO-d_6), δ: 16.1 (Me); 73.3 (C(2)); 106.2 (C(5)); 120.8, 125.8, 132.1, 133.0 (Ar); 136.3 (C(6)); 166.9 (C=O).

Ethyl 2-oxo-5-(4-tolyl)-1,2,3,4-tetrahydropyridine-3-carboxylate (8) and ethyl 2-oxo-5-(4-tolyl)-1,2,3,4-tetrahydropyridine-4-carboxylate (9). *B.* Tetrabutylammonium bromide (8.5 g, 29.4 mmol), azirine **1b** (1 g, 7.63 mmol), ethyl acrylate (2.3 g, 22.9 mmol), and CF_2Br_2 (4.3 mL, 30 mmol) were added to a flask containing freshly prepared lead chips (4.77 g, 22.9 mmol) under a layer of CH_2Cl_2 (40 mL). The flask was closed with a stopper to withstand small excessive pressure. The reaction mixture was stirred at 40—45 °C until the metallic lead completely consumed (6 h) and cooled. A saturated aqueous $NaHCO_3$ solution (100 mL) was added and the products were extracted with CH_2Cl_2 (4×50 mL). The combined extracts were washed with water (2×50 mL) and dried with $MgSO_4$. After removal of the solvent *in vacuo*, column chromatography of the residue on silica gel (hexane—AcOEt, 10 : 2, as the eluent) afforded compounds **8** (0.085 g, 4.3%) and **9** (0.160 g, 8.1 %).

Compound **8**, m.p. 154 °C (from hexane—AcOEt). Found (%): C, 69.53; H, 6.33; N, 5.02. $C_{15}H_{17}NO_3$. Calculated (%): C, 69.48; H, 6.61; N, 5.40. IR ($CHCl_3$), ν/cm^{-1}: 3415 (NH); 1745, 1700 (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.28 (t, 3 H, Me, J = 7.1 Hz); 2.35 (s, 3 H, Me); 2.91 (ddd, 1 H, H(4), J = 16.6 Hz, J = 7.0 Hz, J = 1.2 Hz); 3.23 (ddd, 1 H, H(4), J = 16.6 Hz, J = 9.1 Hz, J = 1.4 Hz); 3.61 (dd, 1 H, H(3), J = 9.1 Hz, J = 7.0 Hz); 4.25 (q, 2 H, CH_2O, J = 7.1 Hz); 6.45 (ddd, 1 H, H(6), J = 4.8 Hz, J = 1.4 Hz, J = 1.2 Hz); 7.15 and 7.23 (both m, 2 H each, Ar, J = 8.3 Hz); 8.32 (br.d, 1 H, NH).

^{13}C NMR ($CDCl_3$), δ: 13.8 and 20.7 (both Me); 26.6 (C(4)); 46.8 (C(3)); 61.4 (CH_2O); 116.7 (C(5)); 120.1 (C(6)); 124.7, 129.0, 134.4, 136.4 (Ar); 166.9, 169.2 (both C=O).

Compound **9**, m.p. 136 °C (from hexane—AcOEt). Found (%): C, 69.49; H, 6.59; N, 5.29. $C_{15}H_{17}NO_3$. Calculated (%): C, 69.48; H, 6.61; N, 5.40. IR ($CHCl_3$), ν/cm^{-1}: 3420, 3230 (NH); 1705, 1665 (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.19 (t, 3 H, Me, J = 7.1 Hz); 2.35 (s, 3 H, Me); 2.82 (dd, 1 H, H(3), J = 16.6 Hz, J = 6.9 Hz); 2.91 (dd, 1 H, H(3), J = 16.6 Hz, J = 3.1 Hz); 3.78 (dd, 1 H, H(4), J = 6.9 Hz, J = 3.1 Hz); 4.15 (q, 2 H, CH_2O, J = 7.1 Hz); 6.61 (d, 1 H, H(6), J = 5.0 Hz); 7.15 and 7.30 (both m, 2 H each, Ar, J = 8.3 Hz); 8.51 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 13.6, 20.7 (both Me); 33.0 (C(4)); 40.5 (C(3)); 61.0 (CH_2O); 114.5 (C(5)); 122.8 (C(6)); 124.5, 129.0, 133.9, 136.3 (Ar); 169.8 and 171.6 (both C=O).

1-Allyloxy-2-(1-isocyanato-2-methylprop-1-enyl)benzene (12). Compound **12** was obtained in a yield of 0.270 g (53%) from 3-(2-allyloxyphenyl)-2,2-dimethyl-2*H*-azirine (**10**) (0.45 g, 2.24 mmol) according to the method *A* (the reaction time was 5 h); chromatography was carried out using a 12 : 1 hexane—AcOEt mixture as the eluent. IR (CCl_4), ν/cm^{-1}: 2260 (N=C=O). ^{1}H NMR ($CDCl_3$), δ: 1.62 and 1.93 (both s, 3 H each, Me); 4.61—4.63 (m, 2 H, OCH_2); 5.30 (d, 1 H, CH_2=, J = 11.4 Hz); 5.42 (d, 1 H, CH_2=, J = 15.4 Hz); 6.02—6.14 (m, 1 H, CH=); 6.93—6.96 and 7.16—7.32 (both m, 2 H each, Ar). ^{13}C NMR ($CDCl_3$), δ: 19.7 and 19.9 (both Me); 68.7 (OCH_2); 112.2, 117.1, 120.2, 121.2, 126.6, 129.2, 130.1, 130.8, 132.4, 132.8, 155.4.

Compound **12** was also prepared in 58% yield from azirine **10** according to the same procedure but without the addition of DMAD.

***N*-[1-(2-Allyloxyphenyl)-2-methylprop-1-enyl]morpholine-4-carboxamide (13).** Morpholine (0.038 g, 0.44 mmol) was added with stirring to a solution of isocyanate **12** (0.100 g, 0.44 mmol) in anhydrous benzene (5 mL). The reaction mixture was kept at ~20 °C for 20 min and concentrated *in vacuo*. After recrystallization, urea **13** was obtained in a yield of 0.128 g (93%), m.p. 107 °C (from diethyl ether). Found (%): C, 68.11; H, 7.66; N, 8.80. $C_{18}H_{24}N_2O_3$. Calculated (%): C, 68.33; H, 7.65; N, 8.85. IR ($CHCl_3$), ν/cm^{-1}: 3440 (NH); 1665 (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.73 and 1.86 (both s, 3 H each, Me); 3.33—3.36 and 3.64—3.67 (both m, 4 H each, OCH_2); 4.85 (d, 2 H, CH_2, J = 5.1 Hz); 5.29 (d, 2 H, CH_2=, J = 11.6 Hz); 5.38 (d, 2 H, CH_2=, J = 16.7 Hz); 6.03 (br.s, 1 H, NH); 6.12—6.44 (m, 1 H, CH=); 6.87—6.98 and 7.21—7.34 (both m, 2 H, Ar each). ^{13}C NMR ($CDCl_3$), δ: 19.5 and 20.7 (both Me); 43.9 (NCH_2); 66.2 and 68.5 (both OCH_2), 111.7, 117.0, 120.3, 125.3, 127.8, 128.0, 130.5, 131.7, 133.1, 155.1, 155.7 (C=O).

9-[Isocyanato(phenyl)methylidene]-9*H*-fluorene (17). Compound **17** was prepared in a yield of 0.450 g (41%) from azirine **15** (1 g, 3.75 mmol) according to the method *A* (the reaction time was 12 h); chromatography was carried out using a 12 : 1 hexane—AcOEt mixture as the eluent, m.p. 123 °C (from hexane). Found (%): C, 85.25; H, 4.38; N, 4.65. $C_{21}H_{13}NO$. Calculated (%): C, 85.40; H, 4.44; N, 4.74. IR ($CHCl_3$), ν/cm^{-1}: 2250 (N=C=O). ^{1}H NMR ($CDCl_3$), δ: 6.49 (d, 1 H, Ar, J = 8.0 Hz); 6.94 (t, 1 H, Ar, J = 8.0 Hz); 7.26 (t, 1 H, Ar, J = 7.3 Hz); 7.40—7.47 (m, 2 H, Ar); 7.56—7.61 (m, 5 H, Ph); 7.71 (d, 1 H, Ar, J = 8.0 Hz); 7.77—7.79 (m, 1 H, Ar); 8.50—8.53 (m, 2 H, Ar). ^{13}C NMR ($CDCl_3$), δ: 119.1, 119.2, 123.7, 124.6, 126.2, 127.1, 127.5, 127.7, 127.8, 128.1, 128.8, 129.3, 129.5, 130.0, 136.5, 136.6, 138.6, 139.3, 140.0.

Compound **17** was also prepared from azirine **15** in 45% yield according to the same procedure but without the addition of DMAD.

***N*-[Phenyl(fluoren-9-ylidene)methyl]piperidine-1-carboxamide (19a).** Piperidine (0.023 g, 0.27 mmol) was added with stirring to a solution of isocyanate **17** (0.080 g, 0.27 mmol) in anhydrous benzene (3 mL). The reaction mixture was kept at ~20 °C for 10 min and then concentrated *in vacuo*. After recrystallization, amide **19a** was obtained in a yield of 0.1 g (98%), m.p. 224—226 °C (from CH_2Cl_2). Found (%): C, 81.85; H, 6.31; N, 7.05. $C_{26}H_{24}N_2O$. Calculated (%): C, 82.08; H, 6.36; N, 7.36. IR ($CHCl_3$), ν/cm^{-1}: 3440, 3390 (NH); 1680 (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.59—1.63 (m, 6 H, CH_2); 3.43—3.45 (m, 4 H, NCH_2); 6.59 (d, 1 H, Ar, J = 8.0 Hz); 6.90 (br.s, 1 H, NH); 6.89—6.94 (m, 1 H, Ar); 7.21 (dt, 1 H, Ar, J = 7.4 Hz, J = 1.1 Hz); 7.34—7.42 (m, 3 H, Ar); 7.46—7.55 and 7.62—7.67 (both m, 2 H each, Ar); 7.73 (dt, 1 H, Ar, J = 7.6 Hz, J = 0.8 Hz); 7.82—7.85 and 7.94—7.97 (both m, 1 H each, Ar). ^{13}C NMR (DMSO-d_6), δ: 24.1, 25.9 (both CH_2); 44.9 (NCH_2); 119.4, 119.5, 122.7, 123.32, 123.8, 124.3, 125.9, 126.2, 126.5, 126.7, 128.3, 128.4, 129.2, 129.9, 137.8, 138.1, 138.6, 138.7, 141.2 (Ar); 154.3 (C=O).

***N*-[Phenyl(fluoren-9-ylidene)methyl]morpholine-4-carboxamide (19b).** Analogously, amide **19b** was prepared from isocyanate **17** (0.080 g, 0.27 mmol) and morpholine (0.024 g, 0.27 mmol) in a yield of 0.100 g (96%), m.p. 221—223 °C (from CH_2Cl_2). Found (%): C, 78.58; H, 5.74; N, 7.33. $C_{25}H_{22}N_2O_2$. Calculated (%): C, 78.51; H, 5.80; N, 7.32. IR ($CHCl_3$), ν/cm^{-1}: 3430, 3380 (NH); 1685 (C=O). ^{1}H NMR ($CDCl_3$), δ: 3.45 (br.s, 4 H, NCH_2); 3.62 (br.s, 4 H, OCH_2); 6.57—6.68 (br.m, 1 H, Ar); 6.91 (br.s, 1 H, NH); 6.82—6.96 (br.m, 1 H, Ar); 7.31—7.42 (br.m, 2 H, Ar); 7.43—7.65 (br.m, 5 H, Ar); 7.66—7.75, 7.76—7.85, and 7.86—7.96 (all br.m, 1 H each, Ar). ^{13}C NMR ($CDCl_3$), δ: 44.5 (NCH_2); 66.2 (OCH_2); 119.0, 119.7, 122.7, 123.0, 123.2, 126.0, 126.4, 126.7, 127.0, 128.4, 129.5, 129.7, 136.6, 137.3, 137.5, 138.8, 139.0, 139.2, 154.6 (C=O).

1-Benzyl-3-[phenyl(fluoren-9-ylidene)methyl]urea (19c). Analogously, amide **19c** was prepared from isocyanate **17** (0.080 g, 0.27 mmol) and benzylamine (0.029 g, 0.27 mmol) in a yield of 0.104 g (95%), m.p. 211—213 °C (from CH_2Cl_2). Found (%): C, 83.62; H, 5.27; N, 6.79. $C_{28}H_{22}N_2O$. Calculated (%): C, 83.56; H, 5.51; N, 6.96. IR ($CHCl_3$), ν/cm^{-1}: 3435, 3395 (NH); 1685 (C=O). ^{1}H NMR ($CDCl_3$), δ: 4.25 (br.s, 2 H, CH_2); 5.30 (br.s, 1 H, NH); 6.63 (br.s, 1 H, Ar); 6.90—8.00 (br.m, 19 H, Ar, NH). ^{13}C NMR ($CDCl_3$), δ: 44.0 (CH_2); 119.1, 119.4, 123.1, 123.7, 124.4, 126.0, 126.7, 126.9, 127.1, 127.3, 128.1, 128.9, 130.1, 136.3, 136.8, 136.9, 137.3, 137.8, 139.1 139.3, 154.6 (C=O).

The reaction of isocyanate **17** (0.080 g, 0.27 mmol) with *N*-benzylidenebenzylamine (0.053 g, 0.27 mmol) under the same conditions (the reaction time was 7 h) afforded amide **19c** (0.098 g, 90%).

(*E*)-Isocyanatostilbene (18). Compound **18** was prepared in a yield of 0.710 g (41%) (its spectroscopic data coincided with those published in the literature[17]) from azirine **16** (1.5 g, 7.77 mmol) according to the method *A* (the reaction time was 5 h); chromatography was carried out using a 12 : 1 hex-

ane—AcOEt mixture as the eluent. Compound **18** was also prepared from azirine **16** (1 g, 5.18 mmol) in a yield of 0.50 g (44 %) according to the method *A* without the addition of DMAD (the reaction time was 5 h).

Dimethyl 2-fluoropyridine-5-(4-methoxyphenyl)-3,4-dicarboxylate (4a). Pyridine **4a** was obtained from azirine **1f** (1 g, 6.80 mmol) according to the method *A* (5 h, sonication) in a yield of 0.781 g (29%); chromatography was carried out using a 8 : 1 hexane—AcOEt mixture as the eluent. IR (CCl_4), ν/cm^{-1}: 1750, 1760 (C=O). ^{1}H NMR ($CDCl_3$), δ: 3.72, 3.85, and 3.95 (all s, 3 H each, MeO); 6.97 and 7.27 (both d, 2 H each, Ar, J = 8.5 Hz); 8.35 (s, 1 H, H(6)). ^{13}C NMR ($CDCl_3$), δ: 52.5, 52.8, and 54.9 (all MeO); 111.5 (d, C(3), $^2J_{C,F}$ = 29.9 Hz); 113.9, 126.4, and 129.4 (all C(Ar)); 133.0 (d, C(5), $^4J_{C,F}$ = 4.6 Hz); 145.0 (C(4)); 150.9 (d, C(6), $^3J_{C,F}$ = 15.0 Hz); 159.3 (d, C(2), $^1J_{C,F}$ = 247 Hz); 159.7 (Ar); 163.0 (d, C=O, $^3J_{C,F}$ = 6.9 Hz); 165.7 (d, C=O, $^4J_{C,F}$ = 2.5 Hz).

Dimethyl 2-fluoropyridine-5-phenyl-3,4-dicarboxylate (4b). A solution of compound **3a** (0.1 g, 0.32 mmol) in $CHCl_3$ (5 mL) was kept at ~20 °C for two weeks. Then the reaction mixture was concentrated. After recrystallization from EtOH, pyridine **4b** was obtained in a yield of 0.09 g (96%), m.p. 66—68 °C (from EtOH). Found (%): C, 62.00; H, 4.24; N, 4.69. $C_{15}H_{12}FNO_4$. Calculated (%): C, 62.28; H, 4.18; N, 4.84. IR (CCl_4), ν/cm^{-1}: 1760, 1750 (C=O). ^{1}H NMR ($CDCl_3$), δ: 3.70 and 3.97 (both s, 3 H each, MeO); 7.33—7.46 (m, 5 H, Ph); 8.38 (s, 1 H, H(6)). ^{13}C NMR ($CDCl_3$), δ: 52.6 and 52.9 (both MeO); 111.7 (d, C(3), $^2J_{C,F}$ = 31.0 Hz); 128.2, 128.4, 128.5, 134.2 (C(Ph)); 133.3 (d, C(5), $^4J_{C,F}$ = 5.5 Hz); 145.1 (d, C(4), $^3J_{C,F}$ = 2.2 Hz); 150.9 (d, C(6), $^3J_{C,F}$ = 15.0 Hz); 159.5 (d, C(2), $^1J_{C,F}$ = 247 Hz); 162.9 (d, C=O, $^3J_{C,F}$ = 6.6 Hz); 165.5 (d, C=O, $^4J_{C,F}$ = 4.4 Hz).

Dimethyl 2-fluoropyridine-5-(4-tolyl)-3,4-dicarboxylate (4c). A solution of compound **3b** (0.1 g, 0.31 mmol) in $CHCl_3$ (5 mL) was kept at ~20 °C for one week. Then the reaction mixture was concentrated. After recrystallization, pyridine **4c** was obtained in a yield of 0.091 g (97%), m.p. 93—95 °C (from hexane—AcOEt). Found (%): C, 63.42; H, 4.76; N, 4.64. $C_{16}H_{14}FNO_4$. Calculated (%): C, 63.36; H, 4.65; N, 4.62. IR (CCl_4), ν/cm^{-1}: 1755 (C=O). ^{1}H NMR ($CDCl_3$), δ: 2.43 (s, 3 H, Me); 3.72 and 3.96 (both s, 3 H each, MeO); 7.21—7.27 (m, 4 H, Ar); 8.36 (s, 1 H, H(6)). ^{13}C NMR ($CDCl_3$), δ: 20.9 (s, Me); 52.5 and 52.9 (both MeO); 111.6 (d, C(3), $^2J_{C,F}$ = 30.4 Hz); 128.1, 129.2, 131.3, 138.5 (C(Ar)); 133.3 (d, C(5), $^4J_{C,F}$ = 4.5 Hz); 145.0 (d, C(4), $^3J_{C,F}$ = 2.8 Hz); 150.9 (d, C(6), $^3J_{C,F}$ = 15.5 Hz); 159.6 (d, C(2), $^1J_{C,F}$ = 247 Hz); 162.9 (d, C=O, $^3J_{C,F}$ = 7.1 Hz); 165.7 (d, C=O, $^4J_{C,F}$ = 3.9 Hz).

A solution of compound **3b** (0.18 g, 0.56 mmol) and TsOH (5 mg) in MeOH (5 mL) was heated at 55 °C for 25 min. Then the reaction mixture was concentrated. Column chromatography of the residue on silica gel (hexane—AcOEt, 10 : 2, as the eluent) afforded pyridine **4c** (0.045 g, 27%).

Dimethyl 5-(4-chlorophenyl)pyridine-2-fluoro-3,4-dicarboxylate (4d). A solution of compound **3c** (0.1 g, 0.29 mmol) in $CHCl_3$ (5 mL) was kept at ~20 °C for 4 months. Then the reaction mixture was concentrated. After recrystallization, pyridine **4d** was obtained in a yield of 0.078 g (83%), m.p. 56 °C (from hexane—AcOEt). Found (%): C, 55.70; H, 3.72; N, 4.31. $C_{15}H_{11}ClFNO_4$. Calculated (%): C, 55.66; H, 3.42; N, 4.33. IR (CCl_4), ν/cm^{-1}: 1755 (C=O). ^{1}H NMR ($CDCl_3$), δ: 3.73 and 3.98 (both s, 3 H each, MeO); 7.29 and 7.45 (both d, 2 H each, Ar, J = 8.4 Hz); 8.36 (s, 1 H, H(6)). ^{13}C NMR ($CDCl_3$), δ: 52.7 and 53.0 (both MeO); 111.7 (d, C(3), $^2J_{C,F}$ = 30.9 Hz); 128.7, 129.6, 132.6, 134.9 (C(Ar)); 132.2 (d, C(5), $^4J_{C,F}$ = 5.5 Hz); 145.1 (d, C(4), $^3J_{C,F}$ = 2.8 Hz); 150.7 (d, C(6), $^3J_{C,F}$ = 15.5 Hz); 159.6 (d, C(2), $^1J_{C,F}$ = 248 Hz); 162.8 (d, C=O, $^3J_{C,F}$ = 6.4 Hz); 165.3 (d, C=O, $^4J_{C,F}$ = 3.9 Hz).

Dimethyl 5-(4-bromophenyl)-2-fluoropyridine-3,4-dicarboxylate (4e). A solution of compound **3d** (0.1 g, 0.26 mmol) in $CHCl_3$ (5 mL) was kept at ~20 °C for 3 months. Then the reaction mixture was concentrated. After recrystallization, pyridine **4e** was obtained in a yield of 0.086 g (91%), m.p. 94 °C (from hexane—diethyl ether). Found (%): C, 48.81; H, 3.44; N, 3.81. $C_{15}H_{11}BrFNO_4$. Calculated (%): C, 48.94; H, 3.01; N, 3.80. IR ($CHCl_3$), ν/cm^{-1}: 1755 (C=O). ^{1}H NMR ($CDCl_3$), δ: 3.73 and 3.97 (both s, 3 H each, MeO); 7.21 and 7.89 (both d, 2 H each, Ar, J = 8.0 Hz); 8.30 (s, 1 H, H(6)). ^{13}C NMR ($CDCl_3$), δ: 52.7 and 53.0 (both MeO); 111.7 (d, C(3), $^2J_{C,F}$ = 31.0 Hz); 123.1, 129.8, 131.6, 133.1 (C(Ar)); 132.2 (d, C(5), $^4J_{C,F}$ = 5.5 Hz); 145.1 (d, C(4), $^3J_{C,F}$ = 2.8 Hz); 150.6 (d, C(6), $^3J_{C,F}$ = 15.5 Hz); 159.6 (d, C(2), $^1J_{C,F}$ = 248 Hz); 162.8 (d, C=O, $^3J_{C,F}$ = 6.6 Hz); 165.4 (d, C=O, $^4J_{C,F}$ = 4.4 Hz).

Dimethyl (4*RS*,5*RS*)-2,4-bis(methylamino)-5-(4-tolyl)-1-azabicyclo[3.1.0]hex-2-ene-3,4-dicarboxylate (21a). A solution of methylamine (29 mg, 0.93 mmol) and triethylamine (0.097 g, 0.96 mmol) in anhydrous benzene (2 mL) was added to a solution of compound **3b** (0.1 g, 0.31 mmol) in benzene (5 mL). The reaction mixture was stirred at ~20 °C, the course of the reaction being monitored by TLC. The product was filtered off and recrystallized to obtain compound **21a** (0.074 g, 69 %). The physicochemical constants and spectroscopic characteristics of compound **21a** coincided with those published earlier.[1]

Dimethyl (4*RS*,5*RS*)-2,4-bis(benzylamino)-5-(4-tolyl)-1-azabicyclo[3.1.0]hex-2-ene-3,4-dicarboxylate (21b). A mixture of benzylamine hydrochloride (0.133 g, 0.93 mmol), triethylamine (0.188 g, 1.86 mmol), and anhydrous benzene (2 mL) was added to a solution of compound **3b** (0.1 g, 0.31 mmol) in benzene (5 mL). The reaction mixture was stirred at ~20 °C, the course of the reaction being monitored by TLC. The product was filtered off and recrystallized to obtain compound **21b** (0.089 g, 58 %), m.p. 104 °C (from hexane—AcOEt). Found (%): C, 72.58; H, 6.30; N, 8.49. $C_{30}H_{31}N_3O_4$. Calculated (%): C, 72.41; H, 6.28; N, 8.44. IR ($CHCl_3$), ν/cm^{-1}: 3400, 3340 (NH); 1740, 1675, 1615 (C=O/C=C). ^{1}H NMR ($CDCl_3$), δ: 2.18 (s, 1 H, H(6)); 2.40 (br.s, 4 H, Me, NH); 2.63 (s, 1 H, H(6)); 3.30 and 3.43 (both d, 2 H each, CH_2N, J = 12.3 Hz); 3.65 and 3.84 (both s, 3 H each, MeO); 4.83—4.95 (m, 2 H, CH_2N); 6.75—6.78 (m, 2 H, Ar); 7.12—7.45 (m, 12 H, Ar); 7.87 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 20.8 (Me); 46.3 (C(6)); 46.6 and 47.0 (both CH_2N); 50.1 and 52.4 (both MeO); 55.5 (C(5)); 72.3 (C(4)); 85.8 (C(3)); 126.1, 126.7, 127.0, 127.1, 127.5, 128.0, 128.4, 128.6, 133.2, 136.8, 138.3, 140.2 (Ar); 167.6 (C(2)); 172.2 and 173.8 (both C=O).

Dimethyl (4*RS*,5*RS*)-2,4-bis[(methoxycarbonylmethyl)amino]-5-phenyl-1-azabicyclo[3.1.0]hex-2-ene-3,4-dicarboxylate (22a) and dimethyl 7-[(methoxycarbonylmethyl)amino]-3-oxo-6-phenyl-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridine-7,8-dicarboxylate (23a). A solution of glycine methyl ester hydrochloride (0.508 g, 4.05 mmol) and triethylamine (0.808 g, 8 mmol) in MeOH (2 mL) was added to a solution of compound **3a** (0.5 g, 1.62 mmol) in MeOH (4 mL). The reaction mixture was stirred

at ~20 °C for 30 min and concentrated *in vacuo*. Column chromatography of the residue on silica gel (hexane—AcOEt, 2 : 1, as the eluent) afforded compounds **22a** (0.212 g, 29%) and **23a** (0.076 g, 11%).

Compound **22a**, m.p. 57—59 °C (from hexane—diethyl ether). Found (%): C, 56.32; H, 5.70; N, 9.35. $C_{21}H_{25}N_3O_8$. Calculated (%): C, 56.37; H, 5.63; N, 9.39. IR ($CHCl_3$), ν/cm^{-1}: 3335 (NH); 1750, 1680, 1630 (C=O/C=C). ^{1}H NMR ($CDCl_3$), δ: 2.18 and 2.73 (both s, 1 H each, H(6)); 2.93 and 3.16 (both d, 1 H each, CH_2N, J = 17.2 Hz); 3.53, 3.67, 3.82, and 3.86 (all s, 3 H each, MeO); 4.32 (dd, 1 H, CH_2N, J = 18.0 Hz, J = 6.0 Hz); 4.48 (dd, 1 H, CH_2N, J = 18.0 Hz, J = 6.4 Hz); 7.30—7.41 (m, 5 H, Ph), 7.67 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 44.0 and 44.1 (both CH_2); 47.3 (C(6)); 50.0, 51.4, 52.1, 52.6 (all MeO); 55.4 (C(5)); 72.0 (C(4)); 86.7 (C(3)); 126.5, 127.3, 128.0, 135.4 (C(Ph)); 167.0 (C(2)); 169.7 (C=O); 171.7 (2 C=O); 173.1 (C=O).

Compound **23a**, m.p. 131 °C (from hexane—CH_2Cl_2). Found (%): C, 57.82; H, 5.14; N, 10.47. $C_{20}H_{21}N_3O_7$. Calculated (%): C, 57.83; H, 5.10; N, 10.12. IR ($CHCl_3$), ν/cm^{-1}: 3430, 3380 (NH); 1755, 1690, 1590 (C=O/C=C). ^{1}H NMR ($CDCl_3$), δ: 2.62 (br.s, 1 H, NH); 3.55 (br.s, 2 H, CH_2); 3.58, 3.73, and 3.77 (all s, 3 H each, MeO); 4.49 and 4.58 (both d, 1 H each, CH_2, J = 17.2 Hz); 5.01 (s, 1 H, H(5)); 7.23—7.38 (m, 5 H, Ph); 8.07 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 44.5 and 45.8 (both CH_2); 51.0, 51.6, and 52.0 (all MeO); 69.7 (C(7)); 78.6 (C(8)); 118.3 (C(6)); 126.6 (C(5)); 127.0, 127.7, 128.1, 137.0 (C(Ph)); 151.7 (C(8a)); 165.5, 168.3, 169.7, and 172.3 (all C=O).

Dimethyl (4*RS*,5*RS*)-2,4-bis[(methoxycarbonylmethyl)amino]-5-(4-tolyl)-1-azabicyclo[3.1.0]hex-2-ene-3,4-dicarboxylate (22b) and dimethyl 7-[(methoxycarbonylmethyl)amino]-3-oxo-6-(4-tolyl)-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridine-7,8-dicarboxylate (23b). A solution of glycine methyl ester hydrochloride (0.489 g, 3.9 mmol) and triethylamine (0.808 g, 8 mmol) in MeOH (2 mL) was added to a solution of compound **3b** (0.5 g, 1.55 mmol) in MeOH (4 mL). The reaction mixture was stirred at ~20 °C for 3 h and concentrated *in vacuo*. Column chromatography of the residue on silica gel (hexane—AcOEt, 2 : 1, as the eluent) afforded compounds **22b** (0.323 g, 45%) and **23b** (0.044 g, 7%).

Compound **22b**, m.p. 106—108 °C (from hexane—diethyl ether). Found (%): C, 57.40; H, 5.88; N, 8.96. $C_{22}H_{27}N_3O_8$. Calculated (%): C, 57.26; H, 5.90; N, 9.11. IR ($CHCl_3$), ν/cm^{-1}: 3335 (NH); 1750, 1680, 1625 (C=O/C=C). ^{1}H NMR ($CDCl_3$), δ: 2.04 (s, 1 H, H(6));), 2.32 (s, 3 H, Me); 2.70 (s, 1 H, H(6)); 2.78 (br.s, 1 H, NH); 2.93 and 3.16 (both d, 1 H each, CH_2N, J = 17.4 Hz); 3.54, 3.66, 3.81, and 3.85 (all s, 3 H each, MeO); 4.32 (dd, 1 H, CH_2N, J = 18.0 Hz, J = 6.1 Hz); 4.46 (dd, 1 H, CH_2N, J = 18.0 Hz, J = 6.4 Hz); 7.12 and 7.27 (both d, 2 H each, H(Ar), J = 8.4 Hz); 7.67 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 20.8 (Me); 44.0 and 44.1 (both CH_2); 47.3 (C(6)); 50.4, 51.3, 52.0, and 52.5 (all MeO); 55.4 (C(5)); 72.1 (C(4)); 86.7 (C(3)); 126.4, 128.7, 132.3, 137.0 (C(Ar)); 167.1 (C(2)); 169.7, 171.8, 171.9, and 173.1 (all C=O).

Compound **23b**, m.p. 131 °C (from hexane—CH_2Cl_2). Found (%): C, 58.71; H, 5.42; N, 9.58. $C_{21}H_{23}N_3O_7$. Calculated (%): C, 58.74; H, 5.40; N, 9.79. IR ($CHCl_3$), ν/cm^{-1}: 3430, 3375 (NH); 1755, 1690, 1590 (C=O/C=C). ^{1}H NMR ($CDCl_3$), δ: 2.34 (s, 3 H, Me); 2.63 (br.s, 1 H, NH); 3.53 (br.s, 2 H, CH_2); 3.59, 3.73, and 3.76 (all s, 3 H each, MeO); 4.46 and 4.55 (both d, 1 H each, CH_2, J = 17.4 Hz); 5.05 (s, 1 H, H(5)); 7.13 (br.s, 4 H, Ar), 8.04 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 20.8 (Me); 44.5 and 45.8 (both CH_2); 51.0, 51.6, and 52.0 (all MeO); 69.7 (C(7)); 78.7 (C(8)); 118.4 (C(6)); 125.4 (C(5)); 126.8, 128.8, 134.0, 137.4 (C(Ar)); 151.6 (C(8a)); 165.5, 168.4, 169.7, and 172.3 (all C=O).

Dimethyl (4*RS*,5*RS*)-5-(4-bromophenyl)-2,4-bis[(methoxycarbonylmethyl)amino]-1-azabicyclo[3.1.0]hex-2-ene-3,4-dicarboxylate (22c). A solution of glycine methyl ester hydrochloride (0.408 g, 3.25 mmol) and triethylamine (0.707 g, 7 mmol) in MeOH (2 mL) was added to a solution of compound **3d** (0.5 g, 1.3 mmol) in MeOH (4 mL). The reaction mixture was stirred at ~20 °C for 5 h and concentrated *in vacuo*. Column chromatography of the residue on silica gel (hexane—AcOEt, 2 : 1, as the eluent) afforded compound **22c** (0.291 g, 43%), m.p. 125—127 °C (from hexane—diethyl ether). Found (%): C, 47.48; H, 4.67; N, 7.89. $C_{21}H_{24}BrN_3O_8$. Calculated (%): C, 47.92; H, 4.60; N, 7.98. IR ($CHCl_3$), ν/cm^{-1}: 3340 (NH); 1750, 1680, 1620 (C=O/C=C). ^{1}H NMR ($CDCl_3$), δ: 2.15 and 2.74 (both s, 1 H each, H(6)); 2.79 (br.s, 1 H, NH); 2.86 and 3.12 (both d, 1 H each, CH_2N, J = 17.4 Hz); 3.56, 3.66, 3.81, and 3.85 (all s, 3 H each, MeO); 4.31 (dd, 1 H, CH_2N, J = 18.0 Hz, J = 6.0 Hz); 4.46 (dd, 1 H, CH_2N, J = 18.0 Hz, J = 6.5 Hz); 7.27—7.30 and 7.42—7.45 (both m, 2 H each, H(Ar)); 7.63 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 43.9 and 44.1 (both CH_2); 47.5 (C(6)); 50.4, 51.4, 52.1, and 52.7 (all MeO); 54.8 (C(5)); 72.0 (C(4)); 86.7 (C(3)); 121.3, 128.4, 131.1, 134.7 (C(Ar)); 166.9 (C(2)); 169.7, 171.3, 171.7, and 172.9 (all C=O).

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