Regioselective addition of cyclic nitrones to Feist´s acid dimethyl ester*

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Cyclic nitrones, *viz.*, tetrahydropyridine 1-oxide, 3,4-dihydroisoquinoline 2-oxide, and 2-methoxycarbonyl-4,5-dihydro-3*H*-pyrrole 1-oxide, regioselectively add to dimethyl 3-methylidenecyclopropane-1,2-dicarboxylate to form 5-spirocyclopropaneisoxazolidines. The latter undergo isomerization upon heating to give the corresponding tetrahydropyridin-4-ols and enaminones.

Key words: nitrones, methylidenecyclopropanes, cycloaddition, isoxazolidines, tetrahydropyridin-1-ols.

The 1,3-dipolar cycloaddition is one of the most convenient tools for designing N,O-containing heterocyclic systems. The high regio- and stereoselectivity of the reaction allows one to selectively create up to three new stereocenters in the molecule in one step. This method was used to synthesize various functionalized isoxazolidines.[1,2] Besides, cycloaddition products easily undergo transformations through the N—O bond cleavage.[3] Methylidenecyclopropanes are active in cycloaddition reactions and react with nitrones to form mixtures of 4- and 5-spirocyclopropaneisoxazolidines.[4] Cyclic five- and six-membered nitrones react with methylidenecyclopropane to give mixtures of regioisomeric 4- and 5-spirocyclopropaneisoxazolidines.[5—8] The presence of alkyl or aryl substituents at the exocyclic carbon atom of methylidenecyclopropane leads to an increase in the percentage of the 4-regioisomer,[9] whereas the presence of electron-withdrawing substituents at the same carbon atom results in the selective formation of 5-spirocyclopropaneisoxazolidines.[10—13] Earlier,[14,15] we have found that the nature of substituents in the three-membered ring of cyclopropenes and methylidenecyclopropanes has an effect on their activity and selectivity in dipolar cycloaddition reactions. In particular, the reactions of C-aryl- and C-amidonitrones with 3-methylidenecyclopropane-1,2-dicarboxylic and 2-benzylidenecyclopropane-1,1-dicarboxylic acid esters gave only 4-regioisomers.[16,17] Hence, the aim of the present study was to investigate the regioselectivity of the addition of cyclic nitrones to methylidenecyclopropane containing electron-withdrawing groups in the three-membered ring.

The reactions of dimethyl 3-methylidenecyclopropane-1,2-dicarboxylate (**1**) (Feist´s acid dimethyl ester) with cyclic C-aldonitrones **2** and **3a**,**b** and C-ketonitrone **4** in benzene upon heating produced diastereomeric mixtures of 5-spirocyclopropaneisoxazolidines (ratios of diastereomers **5´** : **5″** = 5 : 3, **6´a** : **6″a** = 2 : 1, **6´b** : **6″b** = 5 : 3, and **7´** : **7″** = 1 : 0.9) in 71—92% yields (Scheme 1).

The structures and compositions of the resulting cycloadducts were determined based on spectroscopic and elemental analysis data. The ^{1}H NMR spectra of compounds **5** and **6** show doublets of cyclopropane protons, doublets of doublets of methylene protons, and a triplet of the methine group of the isoxazolidine ring. The ^{13}C NMR spectra of these compounds exhibit signals of the methine carbon atoms and the quaternary carbon atom of the cyclopropane ring, as well as signals of the methine and methylene carbon atoms of the isoxazolidine ring. The spectroscopic data suggest that the reactions of cyclic nitrones **2**—**4** with ester **1** gave 5-spirocyclopropaneisoxazolidines rather than their 4-regioisomers.

Diastereomers **6´** and **6″**, **7´** and **7″** were separated by preparative chromatography on silica gel. Attempts to separate diastereomers **5´** and **5″** failed. The stereochemistry of adducts **6´a** and **6″a** was determined by two-dimensional correlation NMR spectroscopy. In the ^{1}H NMR NOESY spectrum of compound **6´a**, there are cross-peaks between the signals of the protons H(10b) and H(1a) and between the signals of the cyclopropane proton H(2´) and the methylene proton H(1b) of the isoxazolidine ring. The spectrum of another isomer (**6″a**) has cross-peaks between the protons H(10b) and H(1b) and between the cyclopropane proton H(2´) and the proton H(1b).

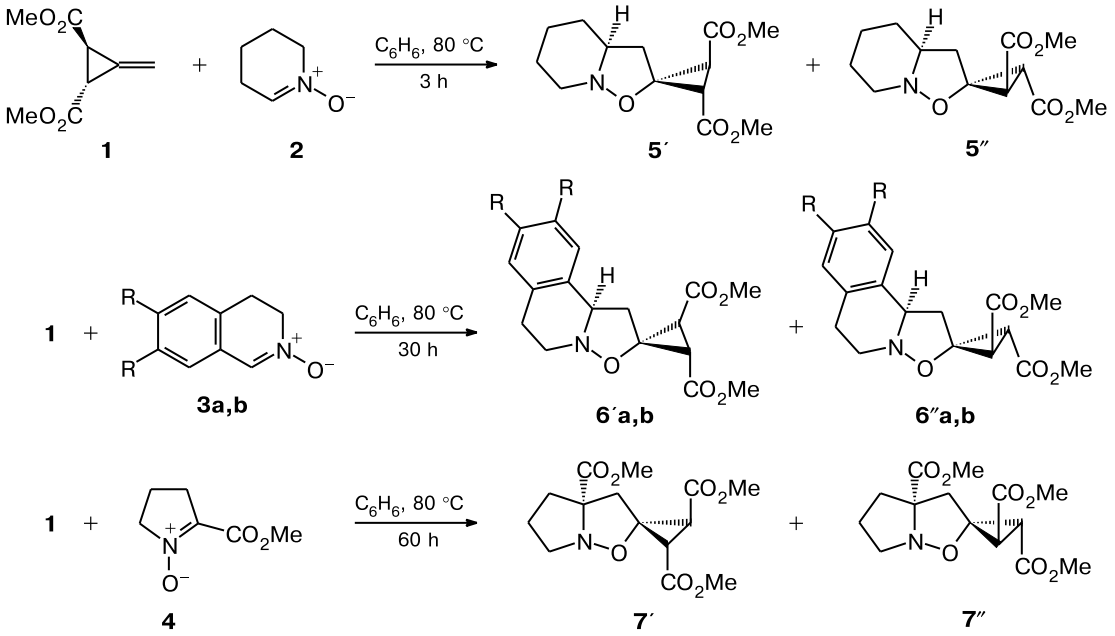
The assignment of the structures of diastereomers **5´**, **5″**, **7´**, and **7″** was made based on the shifts of the signals of the protons of the isoxazolidine and cyclopropane rings in the ^{1}H NMR spectra by analogy with diastereomers **6´** and **6″**.

* Dedicated to Academician of the Russian Academy of Sciences O. M. Nefedov on the occasion of his 80th birthday.

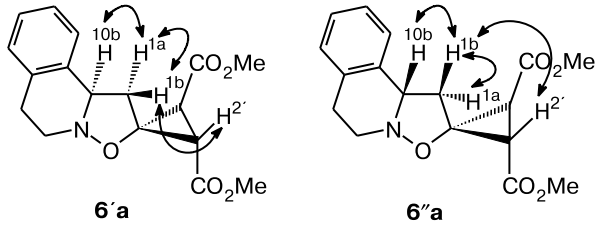
Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 11, pp. 2253—2256, November, 2011.

1066-5285/11/6011-2296

Scheme 1



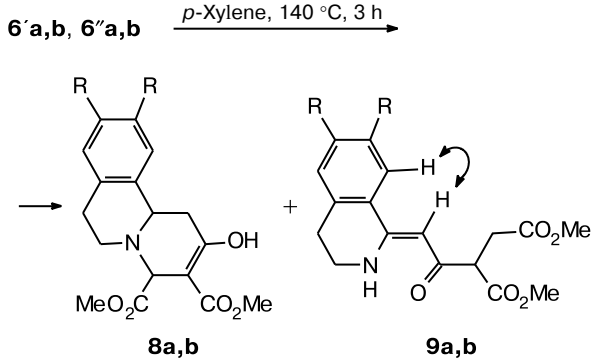
3, **6**: R = H (**a**), MeO (**b**)



It is known[5,18] that 5-spirocyclopropaneisoxazolidines, unlike the corresponding 4-regioisomers, easily undergo the thermal Brandi—Guarna rearrangement to form tetrahydropyridin-4-ones and enaminones. The proposed reaction mechanism involves the homolytic cleavage of the isoxazole ring at the N—O bond followed by the cyclization of the biradical and the formation of the piperidine ring and (or) the hydrogen atom migration and the formation of enaminone. Actually, adducts **6′a**,**b** and **6″a**,**b** are transformed into tetrahydropyridin-4-ols **8a**,**b** and enaminones **9a**,**b** upon heating in *p*-xylene for 2—3 h (Scheme 2). The *Z* configuration of the double bond in enaminone **9a** was established from the two-dimensional correlation ^{1}H NMR NOESY spectrum. Thus, this spectrum shows NOE between the olefinic proton and the proton in the *ortho* position of the aromatic ring.

The thermolysis of one diastereomer **6′a** and of a mixture of two diastereomers **6′a** and **6″a** affords the same compounds. In both cases, tetrahydropyridin-4-ols **8a**,**b** were obtained as the major products (yield 53—71%). Enaminones **9a**,**b** were isolated in 17—19% yields.

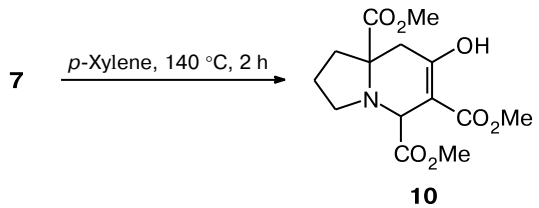
Scheme 2



8, **9**: R = H (**a**), MeO (**b**)

Upon heating in xylene, 5-spirocyclopropaneisoxazolidine **7′** undergoes rearrangement to form tetrahydropyridin-4-ol **10** (yield 59%) as the only diastereomer, whose configuration was not established (Scheme 3).

Scheme 3



Therefore, we found that cyclic nitrones (tetrahydropyridin 1-oxide (**2**), 3,4-dihydroisoquinoline 2-oxides **3a,b**, and 2-methoxycarbonyl-4,5-dihydro-3*H*-pyrrole 1-oxide (**4**)) regioselectively add to dimethyl 3-methylidenecyclopropane-1,2-dicarboxylate (**1**) to form 5-spirocyclopropaneisoxazolidines, which are isomerized to the corresponding tetrahydropyridin-4-ols during heating.

Experimental

The elemental analysis was performed on a Hewlett-Packard 185-B CHN analyzer. The IR spectra of 2% solutions in chloroform were recorded on an UR-20 spectrophotometer. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker DPX-300 instrument (300 and 75 MHz, respectively). The purity and individuality of the compounds were checked and the course of the reactions was monitored by TLC on Silufol UV-254 plates.

Dimethyl 3-methylidenecyclopropane-1,2-dicarboxylate (**1**) was synthesized according to a known procedure.[19] Nitrones **2**—**4** were prepared as described in the study.[20]

Reaction of dimethyl 3-methylidenecyclopropane-1,2-dicarboxylate (1) with cyclic nitrones 2, 3a,b, and 4 (general procedure). A solution of ester **1** (2 mmol) and nitrone **2**, **3a,b**, or **4** (2.2 mmol) was heated in anhydrous benzene (10 mL) at 80 °C for 30 h (in the case of nitrone **4**, the heating was performed for 60 h). Benzene was removed *in vacuo*. Esters **6′a,b**, **6″a,b**, and **7′** were separated by column chromatography on silica gel (a hexane—ethyl acetate mixture was used as the eluent with a gradient from 5 : 1 to 3 : 1). The solvent was evaporated, and the solid compounds were additionally recrystallized. Attempts to separate diastereomers **5′** and **5″** failed.

Dimethyl hexahydrospiro[cyclopropane-1,2′-isoxazolo[2,3-*a*]pyridine]-2,3-dicarboxylate (5). The yield was 385 mg (72%), an inseparable mixture of diastereomers in a ratio of 5 : 3 (^{1}H NMR data), amorphous white powder, R_f 0.31 (AcOEt—hexane, 2 : 3). Found (%): C, 58.15; H, 7.23; N, 5.17. $C_{13}H_{19}NO_5$. Calculated (%): C, 57.98; H, 7.11; N, 5.20. IR, ν/cm^{-1}: 1740 (C=O), 1716 (C=O). Major isomer **5′**. ^{1}H NMR (C_6D_6), δ: 0.79—0.94 (m, 1 H); 1.21—1.58 (m, 5 H); 2.13—2.29 (m, 2 H); 2.37—2.45 and 2.51 (both m, 1 H each); 2.66 (d, 1 H, H(2), J = 6.5 Hz); 2.97—3.06 (m, 1 H); 3.33 (d, 1 H, H(3), J = 6.5 Hz); 3.38 and 3.42 (both s, 3 H each, OMe). ^{13}C NMR (C_6D_6), δ: 24.0, 25.0, and 29.3 (all CH_2); 29.9 (C(2)H); 34.6 (C(3)H); 39.6 (CH_2); 51.8 (2 OMe); 55.8 (C(7′)H_2); 67.5 (C(3a′)); 71.4 (C_{spiro}); 167.6 and 170.2 (both C=O). Minor isomer **5″**. ^{1}H NMR (C_6D_6), δ: 0.79—0.94 (m, 1 H); 1.02—1.13 (m, 2 H); 1.21—1.58 (m, 6 H); 2.13—2.29 and 2.37—2.45 (both m, 1 H each); 2.71 (d, 1 H, H(2), J = 6.5 Hz); 3.28 (d, 1 H, H(3), J = 6.5 Hz); 3.42 and 3.47 (both s, 3 H each, OMe). ^{13}C NMR (C_6D_6), δ: 23.6 and 25.6 (both CH_2); 32.5 (C(2)H); 32.7 (C(3)H); 36.2 and 40.4 (both CH_2); 51.7 and 51.9 (both CH_3); 55.7 (C(7′)H_2); 67.7 (C(3a′)); 71.2 (C_{spiro}); 167.5 and 170.3 (both C=O).

Dimethyl 1′,5′,6′,10b′-tetrahydrospiro[cyclopropane-1,2′-isoxazolo[3,2-*a*]isoquinoline]-2,3-dicarboxylate (diastereomer 6′a). The yield was 361 mg (57%), white powder, m.p. 167—168 °C (from EtOH), R_f 0.52 (AcOEt—hexane, 1 : 1). Found (%): C, 64.61; H, 6.01; N, 4.57. $C_{17}H_{19}NO_5$. Calculated (%): C, 64.34; H, 6.03; N, 4.41. IR, ν/cm^{-1}: 1727 (C=O). ^{1}H NMR (C_6D_6), δ: 2.28 (dd, 1 H, H(1′), J = 13.1 Hz, J = 8.7 Hz); 2.44 (dt, 1 H, H(6′), J = 16.0 Hz, J = 3.6 Hz); 2.51 (d, 1 H, H(2), J = 6.5 Hz); 2.85—2.95 (m, 1 H, H(6′)); 2.90 (dd, 1 H, H(1′), J = 13.1 Hz, J = 8.7 Hz); 3.10—3.18 (m, 2 H, H(5)); 3.33 (d, 1 H, H(3), J = 6.5 Hz); 3.40 and 3.45 (both s, 3 H each, OMe); 4.60 (t, 1 H, H(10b′), J = 8.7 Hz); 6.64 and 6.87 (both d, 1 H each, H_{Ar}, J = 8.0 Hz); 7.03—7.06 (m, 2 H, H_{Ar}). ^{13}C NMR (C_6D_6), δ: 28.3 (C(2)H); 28.7 (C(6′)H_2); 34.8 (C(3)H); 41.1 (C(1′)H_2); 48.4 (C(5′)H_2); 51.8 (2 CH_3O); 63.3 (C(10b′)H); 73.1 (C_{spiro}); 126.7, 127.0, 127.8, and 128.6 (all CH_{Ar}); 133.4 and 135.9 (both C_{Ar}); 167.6 and 170.2 (both C=O).

Dimethyl 1′,5′,6,′10b′-tetrahydrospiro[cyclopropane-1,2′-isoxazolo[3,2-*a*]isoquinoline]-2,3-dicarboxylate (diastereomer 6″a). The yield was 183 mg (29%), glassy substance, R_f 0.37 (AcOEt—hexane, 1 : 1). ^{1}H NMR (C_6D_6), δ: 2.45—2.55 (m, 1 H, CH_2CH_2); 2.58 (dd, 1 H, H(1′), J = 13.1 Hz, J = 8.7 Hz); 2.69—2.76 (m, 1 H, CH_2CH_2); 2.73 (dd, 1 H, H(1′), J = 13.1 Hz, J = 8.7 Hz); 2.79 (d, 1 H, H(3), J = 6.5 Hz); 3.12—3.21 (m, 2 H, CH_2CH_2); 3.24 (s, 3 H, OMe); 3.28 (d, 1 H, H(2), J = 6.5 Hz); 3.48 (s, 3 H, OMe); 4.65 (t, 1 H, H(10b′), J = 8.7 Hz); 6.75 and 6.85 (both d, 1 H each, H_{Ar}, J = 7.3 Hz); 7.00—7.08 (m, 2 H, H_{Ar}). ^{13}C NMR (C_6D_6), δ: 27.8 (C(6′)H_2); 31.5 (C(2)H); 31.6 (C(3)H); 41.3 (C(1′)H_2); 48.9 (C(6′)H_2); 51.7 and 52.1 (both OMe), 62.9 (C(10b′)); 72.8 (C_{spiro}); 126.7, 127.0, 127.7, and 128.8 (all CH_{Ar}); 133.7 and 135.8 (both C_{Ar}); 167.3 and 169.7 (both C=O).

Dimethyl 8,9-dimethoxy-1′,5′,6′,10b′-tetrahydrospiro[cyclopropane-1,2′-isoxazolo[3,2-*a*]isoquinoline]-2,3-dicarboxylate (diastereomer 6′b). The yield was 438 mg (58%), white powder, m.p. 180 °C (from EtOH), R_f 0.23 (AcOEt—hexane, 2 : 3). Found (%): C, 60.48; H, 6.11; N, 3.71. $C_{19}H_{23}NO_7$. Calculated (%): C, 60.47; H, 6.11; N, 3.71. IR, ν/cm^{-1}: 1733 (C=O). ^{1}H NMR (C_6D_6), δ: 2.47 (dd, 1 H, H(1′), J = 13.1 Hz, J = 8.7 Hz); 2.48—2.53 (m, 1 H, CH_2CH_2); 2.59 (d, 1 H, H(2), J = 6.5 Hz); 2.87—2.96 (m, 1 H, CH_2CH_2); 3.02 (dd, 1 H, H(1′), J = 13.1 Hz, J = 8.7 Hz); 3.17—3.23 (m, 1 H, CH_2CH_2); 3.28—3.32 (m, 1 H, CH_2CH_2); 3.33 (d, 1 H, H(3), J = 6.5 Hz); 3.44, 3.47, 3.50, and 3.53 (all s, 3 H each, OMe); 4.65 (t, 1 H, H(10b′), J = 8.7 Hz); 6.29 and 6.42 (both s, 1 H each, H_{Ar}). ^{13}C NMR (C_6D_6), δ: 28.4 (C(6′)H_2); 28.5 (C(2)H); 34.9 (C(3)H); 41.3 (C(1′)H_2); 48.7 (C(5′)H_2); 51.9 (2 OMe); 55.8 and 55.9 (both OMe); 63.2 (C(10b′)H); 73.3 (C_{spiro}); 111.1 and 112.2 (both CH_{Ar}); 125.4 and 127.6 (both C_{Ar}); 149.3 (2 C_{Ar}); 167.7 and 170.3 (both C=O).

Dimethyl 8,9-dimethoxy-1′,5′,6′,10b′-tetrahydrospiro[cyclopropane-1,2′-isoxazolo[3,2-*a*]isoquinoline]-2,3-dicarboxylate (diastereomer 6″b). The yield was 262 mg (34%), R_f 0.23 (AcOEt—hexane, 2 : 3), glassy substance. ^{1}H NMR (C_6D_6), δ: 2.45—2.74 (m, 2 H, CH_2CH_2); 2.68 (dd, 1 H, H(1′), J = 13.1 Hz, J = 8.7 Hz); 2.73 (dd, 1 H, H(1′), J = 13.1 Hz, J = 8.7 Hz); 2.84 (d, 1 H, H(2), J = 6.5 Hz); 3.21—3.35 (m, 2 H, CH_2CH_2); 3.29 (s, 3 H, OMe); 3.31 (d, 1 H, H(3), J = 6.5 Hz); 3.47, 3.50, and 3.51 (all s, 3 H each, OMe); 4.64 (t, 1 H, H(10b′), J = 8.7 Hz); 6.29 and 6.35 (both s, 1 H each, H_{Ar}). ^{13}C NMR (C_6D_6), δ: 27.5 (C(6′)H_2); 31.5 (C(2)H); 31.7 (C(3)H); 41.3 (C(1′)H_2); 49.2 (C(5′)H_2); 51.7, 52.1, 55.8, and 55.9 (all OMe); 62.8 (C(10b′)H); 73.0 (C_{spiro}); 111.0 (C_{Ar}); 112.3 (CH_{Ar}); 125.7, 127.4, 149.2, and 149.3 (all C_{Ar}); 167.3 and 169.9 (both C=O).

Trimethyl 5,6-dihydro-3*H*,4*H*-spiro[cyclopropane-1,2′-pyrrolo[1,2-*b*]isoxazole]-2,3,3a′-tricarboxylate (7). Major isomer **7′**. The yield was 233 mg (37%), white powder, m.p. 122—123 °C (from EtOH), R_f 0.40 (AcOEt—hexane, 3 : 2). Found (%): C, 53.61; H, 6.12; N, 4.61. $C_{14}H_{19}NO_7$. Calculat-

ed (%): C, 53.67; H, 6.11; N, 4.47. IR (KBr), ν/cm^{-1}: 1728 (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.83—1.94 (m, 1 H, CH_2CH_2); 2.01—2.08 (m, 2 H, CH_2CH_2); 2.31—2.39 (m, 1 H, CH_2CH_2); 2.44 (d, 1 H, H(3′), *J* = 13.8 Hz); 2.52 (d, 1 H, H(2), *J* = 6.5 Hz); 2.83 (d, 1 H, H(3′), *J* = 6.5 Hz); 3.17—3.22 (m, 2 H, CH_2CH_2); 3.20 (d, 1 H, H(3′), *J* = 13.8 Hz); 3.71, 3.72, and 3.73 (all s, 3 H each, OMe). ^{13}C NMR ($CDCl_3$), δ: 24.7 (CH_2); 29.7 (C(2)H); 32.1 (C(3)H); 35.8 and 43.0 (both CH_2); 52.6, 52.8, and 53.2 (all OMe); 58.0 (CH_2); 72.4 (C_{spiro}); 77.6 (C(3a′)); 167.9, 170.2, and 173.6 (all C=O). Minor isomer **7″**. The yield was 210 mg (34%), white powder, m.p. 80—81 °C (from EtOH), R_f 0.27 (AcOEt—hexane, 3 : 2). Found (%): C, 53.72; H, 6.10; N, 4.64. $C_{14}H_{19}NO_7$. Calculated (%): C, 53.67; H, 6.11; N, 4.47. IR ($CHCl_3$), ν/cm^{-1}: 1730 (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.85—1.93 (m, 2 H, CH_2CH_2); 2.00—2.12 and 2.29—2.38 (both m, 1 H each, CH_2CH_2); 2.44 (d, 1 H, H(2), *J* = 6.5 Hz); 2.45 (d, 1 H, H(3′), *J* = 13.8 Hz); 2.89 (d, 1 H, H(3), *J* = 6.5 Hz); 3.13 (d, 1 H, H(3′), *J* = 13.8 Hz); 3.14—3.23 and 3.36—3.44 (both m, 1 H each, CH_2CH_2); 3.72 (s, 6 H, 2 OMe); 3.78 (s, 3 H, OMe). ^{13}C NMR ($CDCl_3$), δ): 24.9 (CH_2); 29.6 (C(2)H); 30.0 (C(3)H); 32.2 and 43.3 (both CH_2); 52.7, 52.8, and 53.3 (all OMe); 58.2 (CH_2); 71.7 and 77.5 (both C_{Ar}); 167.7, 170.0, and 173.6 (all C=O).

Thermolysis of 5-spirocyclopropaneisoxazolidines 6′a,b, 6″a,b, and 7′ (general procedure). A solution of a mixture of two diastereomers of 5-spirocyclopropaneisoxazolidines **6′a**, **6″a** or **6′b**, **6″b** or diastereomer **7′** (2 mmol) was heated in anhydrous *p*-xylene (10 mL) at 140 °C for 2—3 h. Xylene was removed *in vacuo*. The products were separated by preparative chromatography on silica gel (a hexane—AcOEt mixture as the eluent). The solvent was evaporated, and the solid residue was additionally recrystallized.

Dimethyl 2-hydroxy-4,6,7,11b-tetrahydro-1*H*-pyrido-[2,1-*a*]isoquinoline-3,4-dicarboxylate (8a). The yield was 450 mg (71%), white powder, m.p. 102—103 °C (from hexane), R_f 0.57 (AcOEt—hexane, 1 : 2). Found (%): C, 64.64; H, 6.00; N, 4.72. $C_{17}H_{19}NO_5$. Calculated (%): C, 64.34; H, 6.03; N, 4.41. IR, ν/cm^{-1}: 3420 (OH), 1725 (C=O). ^{1}H NMR ($CDCl_3$), δ: 2.46 (dd, 1 H, H(1), *J* = 18.2 Hz, *J* = 10.9 Hz); 2.72 (td, 1 H, CH_2CH_2, *J* = 10.9 Hz, *J* = 3.6 Hz); 2.78—2.88 (m, 1 H, CH_2CH_2); 2.84 (dd, 1 H, H(1), *J* = 18.2 Hz, *J* = 4.4 Hz); 3.01—3.11 (m, 1 H, CH_2CH_2); 3.20 (td, 1 H, CH_2CH_2, *J* = 8.0 Hz, *J* = 4.4 Hz); 3.74 and 3.79 (both s, 3 H each, OMe); 4.38 (s, 1 H, H(4)); 4.43 (dd, 1 H, H(11b), *J* = 10.2 Hz, *J* = 4.4 Hz); 7.10—7.23 (m, 4 H, H_{Ar}); 12.11 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 30.4, 36.5, and 48.0 (all CH_2); 52.0 and 52.1 (both OMe); 52.2 (C(4)H); 62.5 (C(11b)H); 96.8 (C(3)); 126.3, 126.6, 126.7, and 129.4 (all CH_{Ar}); 134.3 and 137.4 (both C_{Ar}); 171.1 and 171.9 (both C=O); 172.3 (C(2)).

Dimethyl 2-hydroxy-9,10-dimethoxy-4,6,7,11b-tetrahydro-1*H*-pyrido[2,1-*a*]isoquinoline-3,4-dicarboxylate (8b). The yield was 400 mg (53%), white powder, m.p. 150—152 °C (from hexane), R_f 0.31 (AcOEt—hexane, 2 : 3). Found (%): C, 60.43; H, 6.15; N, 3.77. $C_{19}H_{23}NO_7$. Calculated (%): C, 60.47; H, 6.14; N, 3.71. IR, ν/cm^{-1}: 1740 (C=O). ^{1}H NMR (C_6D_6), δ: 2.51—2.62 (m, 2 H, H(1) + CH_2CH_2); 2.73—2.82 (m, 2 H, CH_2CH_2); 2.90—3.00 (m, 1 H, H(1)); 3.17 (dt, 1 H, CH_2CH_2, *J* = 10.9 Hz, *J* = 4.4 Hz); 3.41 and 3.47 (both s, 3 H each, OMe); 3.53 (s, 6 H, OMe); 4.56 (s, 1 H, H(4)); 4.63 (dd, 1 H, H(11b), *J* = 10.2 Hz, *J* = 4.4 Hz); 6.32 and 6.49 (both s, 1 H each, H_{Ar}); 12.84 (s, 1 H, OH). ^{13}C NMR (C_6D_6), δ: 30.1 (C(7)H_2); 36.8 (C(1)H_2); 48.5 (C(6)H_2); 51.3 and 51.5 (both OMe); 51.9 (C(11b)H); 55.8 and 55.9 (both OMe); 62.9 (C(4)H); 97.1 (C(3)); 110.0 and 112.7 (both CH_{Ar}); 126.3, 129.7, 149.0, and 149.1 (all C_{Ar}); 171.5 and 171.7 (both C=O); 173.1 (C(2)).

Dimethyl 2-[2-(3,4-dihydroisoquinolin-1(2*H*)-ylidene)-acetyl]succinate (9a). The yield was 120 mg (19%), yellow powder, m.p. 89—90 °C (from hexane), R_f 0.52 (AcOEt—hexane, 2 : 3). Found (%): C, 64.33; H, 6.06; N, 4.47. $C_{17}H_{19}NO_5$. Calculated (%): C, 64.34; H, 6.03; N, 4.41. IR (KBr), ν/cm^{-1}: 3220 (NH), 1740, 1728 (C=O). ^{1}H NMR ($CDCl_3$), δ: 2.87—2.96 (m, 3 H); 3.05 (dd, 1 H, H(3), *J* = 17.4 Hz, *J* = 8.7 Hz); 3.44—3.52 (m, 2 H, CH_2); 3.70 and 3.75 (both s, 3 H each, OMe); 3.96 (dd, 1 H, H(2), *J* = 8.7 Hz, *J* = 6.5 Hz); 5.75 (s, 1 H, H(2′)); 7.23 (d, 1 H, H_{Ar}, *J* = 7.3 Hz); 7.33 (td, 1 H, H_{Ar}, *J* = 7.3 Hz, *J* = 1.4 Hz); 7.43 (td, 1 H, H_{Ar}, *J* = 7.3 Hz, *J* = 1.4 Hz); 7.71 (d, 1 H, H_{Ar}, *J* = 7.3 Hz); 11.20 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 28.5 (C(4′)H_2); 33.8 (C(3)H_2); 39.0 (C(3′)H_2); 52.3 and 52.9 (both OMe); 53.8 (C(2)H); 88.9 (C(2′)H); 126.2, 127.6, and 128.7 (all CH_{Ar}); 129.0 (C_{Ar}); 131.9 (CH_{Ar}); 137.1 and 159.2 (both C_{Ar}); 171.5, 172.8, and 189.6 (all C=O).

Dimethyl 2-[2-(3,4-dihydro-6,7-dimethoxyisoquinolin-1(2*H*)-ylidene)acetyl]succinate (9b). The yield was 128 mg (17%), yellow powder, m.p. 133—134 °C (from hexane), R_f 0.21 (AcOEt—hexane, 2 : 3). Found (%): C, 60.35; H, 6.17; N, 3.76. $C_{19}H_{23}NO_7$. Calculated (%): C, 60.47; H, 6.14; N, 3.71. IR, ν/cm^{-1}: 1750 (C=O). ^{1}H NMR ($CDCl_3$), δ: 2.83—2.93 (m, 3 H); 3.05 (dd, 1 H, H(3), *J* = 17.4 Hz, *J* = 8.7 Hz); 3.42—3.51 (m, 2 H, CH_2); 3.70, 3.75, 3.93, and 3.95 (all s, 3 H each, OMe); 3.90—4.00 (m, 1 H, H(2)); 5.62 (s, 1 H, H(2′)); 6.69 and 7.14 (both s, 1 H each, H_{Ar}); 11.20 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 28.1 (C(4′)H_2); 33.9 (C(3)H_2); 39.1 (C(3′)H_2); 52.3 and 52.9 (both OMe); 53.7 (C(2)H); 56.4 and 56.6 (both OMe); 88.4 (C(2′)H); 109.0 and 111.1 (both CH_{Ar}); 121.0, 131.1, 148.4, 152.4, and 159.3 (all C_{Ar}); 171.6, 173.0, and 189.0 (all C=O).

Trimethyl 7-hydroxy-1,2,3,5,8,8a-hexahydroindolizine-5,6,8a-tricarboxylate (10) was synthesized from adduct **7′** (300 mg, 0.06 mmol), the yield was 178 mg (59%), white powder, m.p. 72—73 °C (from EtOH), R_f 0.20 (AcOEt—hexane, 1 : 3). Found (%): C, 53.75; H, 6.12; N, 4.48. $C_{14}H_{19}NO_7$. Calculated (%): C, 53.67; H, 6.11; N 4.47. IR ($CHCl_3$), ν/cm^{-1}: 3440 (OH), 1738 (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.79—1.93 (m, 2 H); 1.99—2.11 and 2.19–2.27 (both m, 1 H each); 2.32 (d, 1 H, H(8), *J* = 18.2 Hz); 2.96 (dd, 1 H, H(3), *J* = 15.3 Hz, *J* = 8.0 Hz); 3.10 (d, 1 H, H(8), *J* = 18.2 Hz); 3.44 (td, 1 H, H(3), *J* = 8.7 Hz, *J* = 4.4 Hz); 3.67, 3.69, and 3.74 (all s, 3 H each, OMe); 4.39 (s, 1 H, H(5)); 12.14 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 21.7 (C(2)H_2); 33.6 (C(8)H_2); 39.3 (C(1)H_2); 52.1, 52.4, and 52.7 (all OMe); 52.9 (C(4)H_2); 57.6 (C(5)H); 64.8 (C(8a)); 95.1 (C(6)); 171.2, 171.4, and 171.6 (all C=O); 175.1 (C(7)).

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Received June 6, 2011;
in revised form October 7, 2011