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Synthesis of 2,3-diaryl-2,3,4,4a-tetrahydro-5*H*-indeno[1,2-*c*]pyridazin-5-ones

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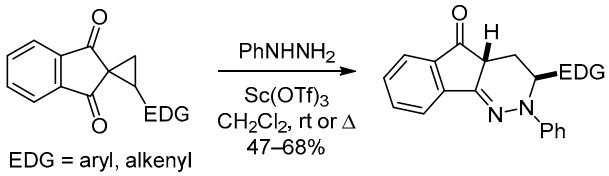


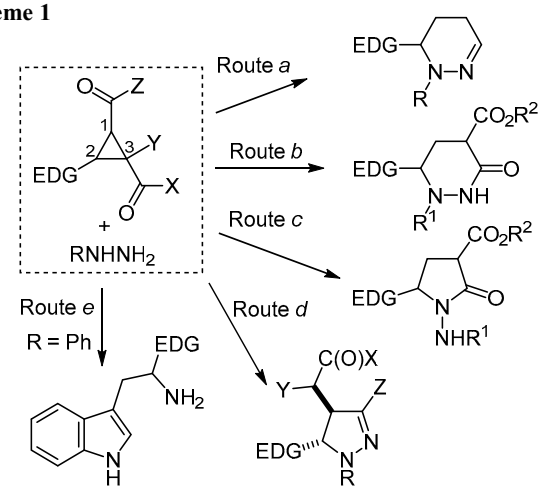
The reaction of 1,3-indanedione-derived donor-acceptor cyclopropanes with phenylhydrazine in the presence of catalytic amounts of scandium trifluoromethanesulfonate leads to the formation of indeno[1,2-*c*]pyridazine derivatives.

Keywords: 2,3,4,4a-tetrahydro-5*H*-indeno[1,2-*c*]pyridazin-5-ones, donor-acceptor cyclopropanes, phenylhydrazine, nucleophilic cleavage.

Cyclopropanes containing donor and acceptor substituents in vicinal positions are unique compounds exhibiting high reactivity with respect to nucleophiles, electrophiles, radicals, dipolarophiles, 1,3-dipoles, 1,3-dienes, and other types of reagents. Thanks to this they have become distinguished as a separate subclass of small rings, called "donor-acceptor cyclopropanes".[1,2] Ease of synthesis, stability, and at the same time high reactivity when activated by Lewis acids make donor-acceptor (DA) cyclopropanes important building blocks in the synthesis of various carbo-[3] and heterocycles,[3d,e,4] including complex polycyclic systems[5] and natural compounds.[6]

In particular, the reaction of DA cyclopropanes with hydrazines, depending on the structure of the reagents and the conditions of the reactions, resulted in different heterocyclic compounds (Scheme 1). If the cyclopropane is sufficiently activated, hydrazines attack not only the carbonyl group of the acceptor substituent, but also the C-2 atom of the small ring to form pyridazine (Scheme 1, routes *a*, *b*)[7] or 1-aminopyrrolidin-2-one derivatives (Scheme 1, route *c*).[7b] Furthermore, 2-arylcyclopropane-1,1-dicarboxylates containing an additional carbonyl group at the C-3 atom reacted with hydrazines with the participation of this group, forming pyrazole derivatives (Scheme 1, route *d*).[8] On the other hand, if cyclopropane is not active enough, as in the

Scheme 1



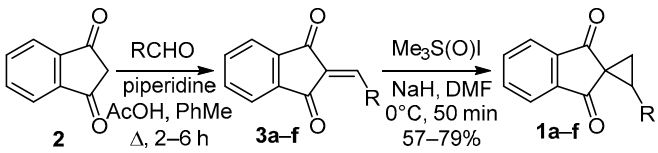
case of alkyl-2-arylcyclopropyl ketones, hydrazines efficiently react only at the carbonyl group and the reaction products are hydrazones[8c,9] or, in the case of phenylhydrazine, the corresponding indole, formed as a result of Fischer rearrangement (Scheme 1, route *e*).[7c,10]

In this work, we studied the reaction of phenylhydrazine with DA cyclopropanes obtained from 1,3-indanedione. Considering the high reactivity of these substrates with respect to nucleophiles[11] and our previous results on studying the reactions of phenylhydrazine with 2-arylcyclopropane-1,1-dicarboxylates,[7b] we expected the formation of indeno[1,2-*c*]pyridazine derivatives which are promising compounds for medicinal chemists and pharmacologists. Thus, the tautomeric 2,4,4a,5-tetrahydroindeno[1,2-*c*]pyridazin-3-ones were found to possess antihypertensive, antithrombotic, and inotropic activity.[12] They inhibit STAT3 protein, which is one of the promising molecular targets in cancer therapy,[13] and exhibit other types of biological activity.[14] In addition, the corresponding aromatic derivatives, 3-arylindeno[1,2-*c*]pyridazin-5-ones, selectively inhibit monoamine oxidase B.[15]

At the first stage of the work, we synthesized a series of 2-aryl(alkenyl)spiro[cyclopropane-1,2'-indane]-1',3'-diones **1a**–**f** using a sequence of transformations involving the reaction of indane-1,3-dione (**2**) with corresponding aldehyde[16] followed by cyclopropanation of the Knoevenagel adducts **3a**–**f** by the Corey–Chaykovsky reaction[17] (Scheme 2).

The structure of compound **1a** was proved by single crystal X-ray analysis (Fig. 1). It should be noted that the length of the C(1)–C(2) bond in the three-membered ring between the carbon atom linked to two carbonyl groups and a carbon atom bearing a phenyl substituent (1.561 Å) is much longer than the C–C bond in unsubstituted cyclopropane (1.513 Å).[18]

Scheme 2



a R = Ph, **b** R = 4-MeC$_6$H$_4$, **c** R = 4-MeOC$_6$H$_4$, **d** R = 4-FC$_6$H$_4$, **e** R = 3,4,5-(MeO)$_3$C$_6$H$_2$, **f** R = 4-MeOC$_6$H$_4$CH=CH

In accordance with our expectations, 2-phenylspiro[cyclopropane-1,2'-indane]-1',3'-dione **1a** was converted to tetrahydroindeno[1,2-*c*]pyridazin-5-one **4a** under the conditions previously optimized for the reaction of phenylhydrazine with 2-arylcyclopropane-1,1-diesters (refluxing in CH_2Cl_2 in the presence of 20 mol % $Ni(ClO_4)_2 \cdot 6H_2O$),[7b] albeit in a low yield. Varying the conditions of the model reaction showed that product **4a** can be obtained in a moderate yield by heating cyclopropane **1a** with 1.1 equiv phenylhydrazine in tetrahydrofuran at 100°C. The best results were obtained when carrying out the reaction in CH_2Cl_2 at room temperature using $Sc(OTf)_3$ as the catalyst.

We carried out the reactions of phenylhydrazine with a series of DA cyclopropanes **1a**–**f** under these conditions

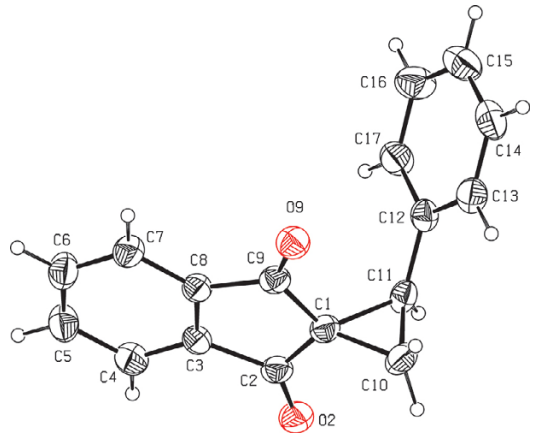
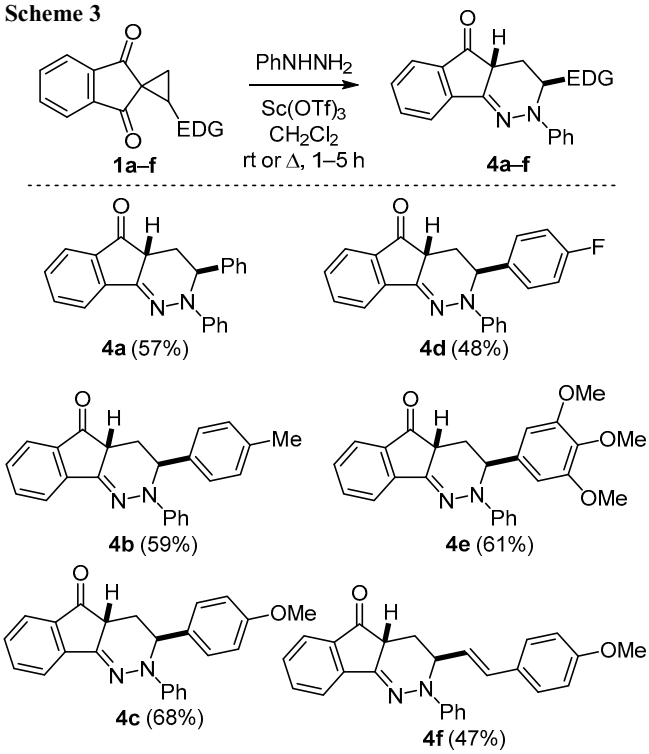


Figure 1. Molecular structure of compound **1a** with atoms represented as thermal vibration ellipsoids with 50% probability.

and obtained the corresponding derivatives of indeno[1,2-*c*]-pyridazine **4a**–**f** (Scheme 3). The yields of the desired products **4a**–**f** generally correlate well with the donor properties of the aromatic substituent; the low yield of compound **4f** with a 4-methoxystyryl substituent is apparently due to side reactions of the highly active cyclopropane **1f**.

The tricyclic products **4a**-**f** are formed as isomers with the *trans* arrangement of substituents at C-3 and C-4a atoms. This conclusion was made on the basis of comparison of the coupling constants for aliphatic protons with those of related compounds,[19] as well as the values obtained as a result of optimization of the geometry of compounds **4a**–**f** by quantum-chemical calculations (see Supplementary information file). In addition, the structure of compound **4a** was unambiguously proven by single crystal X-ray analysis (Fig. 2).

Scheme 3



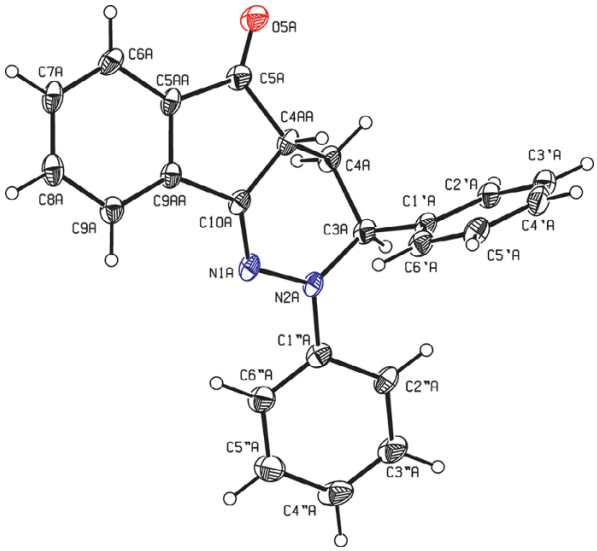


Figure 2. Molecular structure of compound **4a** with atoms represented as thermal vibration ellipsoids with 50% probability.

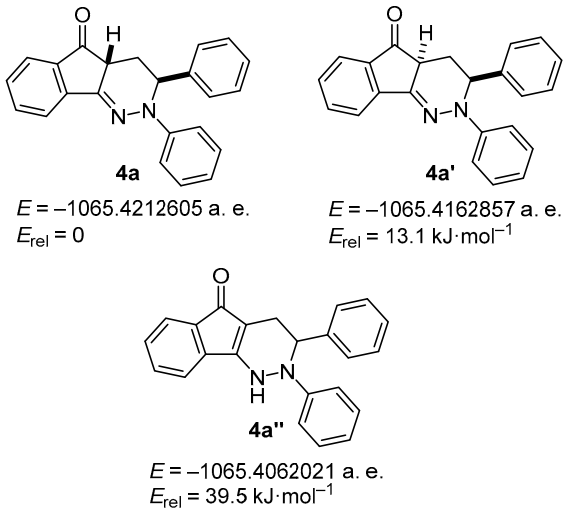


Figure 3. The calculated (HF/6-311G**) absolute and relative energies of compound **4a**, its *cis*-isomer **4a'**, and enehydrazino ketone **4a''**.

Compounds **4a**–**f** do not undergo epimerization or isomerization to enehydrazino ketones, which means that they are thermodynamically controlled products. Indeed, quantum-chemical calculations using the HF/6-311G** method showed that the model compound **4a** is more stable than *cis*-isomer **4a'** and the corresponding enehydrazino ketone **4a''** by 13.1 and 39.5 kJ/mol, respectively (Fig. 3, see Supplementary information file).

To conclude, the scandium triflate-catalyzed reaction of spiro[cyclopropane-1,2'-indane]-1',3'-diones containing a donor aromatic or alkenyl substituent in the three-membered ring with phenylhydrazine leads to the formation of 2,3-substituted 2,3,4,4a-tetrahydro-5*H*-indeno-[1,2-*c*]pyridazin-5-ones in moderate to good yields.

Experimental

IR spectra were registered on an Infralum FT-801 spectrometer in KBr pellets. ^{1}H, ^{13}C and NOESY 2D NMR spectra were acquired on a Bruker Avance-500 (500 and 126 MHz, respectively) spectrometer in $CDCl_3$, using residual solvent signals (7.26 ppm for ^{1}H nuclei, 77.2 ppm for ^{13}C nuclei) to assign chemical shifts. High-resolution mass spectra were recorded on an LTQ Orbitrap Elite spectrometer with samples as MeCN–H_2O solutions, calibration with HCO_2Na–HCO_2H, electrospray ionization. Elemental analysis was performed on a Fisons EA-1108 analyzer. Melting points were determined on an Electrothermal IA9100 apparatus.

Knoevenagel adducts **3a**–**f** were obtained following a published method.[16]

Synthesis of spiro[cyclopropane-1,2'-indane]-1',3'-diones 1a–f (General method).[16] Trimethylsulfoxonium iodide (1.05 equiv) was added in one portion to a stirred suspension of NaH (60% dispersion in mineral oil, 1.05 equiv) in anhydrous DMF (1.25 ml per 1 mmol NaH) at room temperature under argon atmosphere. The reaction mixture was stirred for 45 min, thereafter the formed solution was added dropwise to a prepared 0.33 M solution of alkene **3a**–**f** (1.0–1.8 mmol, 1 equiv) in DMF under argon atmosphere at 0°C. The reaction mixture was stirred for 50 min at 0°C, then poured into aqueous NH_4Cl with ice (10–15 ml) and extracted with EtOAc (5×5 ml). The combined organic layers were washed with H_2O (5×5 ml) followed by saturated aqueous NaCl (1×5 ml), and dried with Na_2SO_4. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel.

2-Phenylspiro[cyclopropane-1,2'-indane]-1',3'-dione (1a). Yield 285 mg (77%), light-yellow crystals, mp 130–132°C (mp 126–128°C,[20] mp 129–131°C,[21] mp 133–134°C[22]). The spectral data correspond to the literature.[20,21]

2-(4-Methylphenyl)spiro[cyclopropane-1,2'-indane]-1',3'-dione (1b). Yield 224 mg (61%), light-yellow crystals, mp 120–122°C (mp 90–92°C,[20] mp 126–128°C[22]). The spectral data correspond to the literature.[21]

2-(4-Methoxyphenyl)spiro[cyclopropane-1,2'-indane]-1',3'-dione (1c). Yield 240 mg (79%), yellow crystals, mp 145–147°C (mp 148–150°C[20]). The spectral data correspond to the literature.[20]

2-(4-Fluorophenyl)spiro[cyclopropane-1,2'-indane]-1',3'-dione (1d). Yield 212 mg (57%), colorless crystals, mp 147–148°C (mp 150–151 °C[20]). The spectral data correspond to the literature.[20]

2-(3,4,5-Trimethoxyphenyl)spiro[cyclopropane-1,2'-indane]-1',3'-dione (1e). Yield 274 mg (75%), light-yellow crystals, mp 132–134 °C, R_f 0.68 (petroleum ether – EtOAc, 1:1). IR spectrum, ν, cm^{-1}: 2990, 2935, 2835, 1740, 1705, 1590, 1510, 1460, 1420, 1385, 1330, 1245, 1130, 1000, 855, 760, 720. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.21–2.25 (1H, m, CH_2); 2.36–2.40 (1H, m, CH_2); 3.27–3.31 (1H, m, CH); 3.77 (3H, s, OCH_3); 3.78 (6H, s, 2OCH_3); 6.51 (2H, s, H Ar); 7.65–7.71 (2H, m, H Ar); 7.72–7.76 (1H, m, H Ar); 7.85–7.90 (1H, m, H Ar). ^{13}C NMR spectrum, δ, ppm: 22.6 (CH_2); 41.7 (CH); 42.9 (C); 56.0 (2OCH_3); 60.7 (OCH_3); 106.3 (2CH); 122.3 (2CH); 129.2 (C); 134.6 (CH); 134.8 (CH); 137.6 (C); 141.4 (C); 142.6 (C); 152.7 (2C); 195.6 (CO); 197.8 (CO). Found, *m*/*z*: 361.1043 [M+Na]$^+$. $C_{20}H_{18}NaO_5$. Calculated, *m*/*z*: 361.1046.

(*E*)-2-[2-(4-Methoxyphenyl)ethenyl]spiro[cyclopropane-1,2'-indane]-1',3'-dione (1f). Yield 220 mg (61%), light-yellow crystals, mp 128–129°C, R_f 0.77 (petroleum ether – EtOAc, 1:1). IR spectrum, ν, cm^{-1}: 2955, 2924, 2855, 1740, 1705, 1605, 1575, 1510, 1465, 1335, 1300, 1250, 1175, 1030, 965, 815, 735. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.10 (1H, dd, ^3J = 8.1, ^2J = 4.1, CH_2); 2.23 (1H, dd, ^3J = 8.7, ^2J = 4.1, CH_2); 2.94–3.00 (1H, m, CH); 3.79 (3H, s, OCH_3); 6.30 (1H, dd, ^3J = 15.9, ^3J = 9.6, CH=); 6.55 (1H, d, ^3J = 15.9, CH=); 6.82 (2H, d, ^3J = 8.7, H Ar); 7.29 (2H, d, ^3J = 8.7, H Ar); 7.75–7.79 (2H, m, H Ar); 7.89–7.96 (2H, m, H Ar). ^{13}C NMR spectrum, δ, ppm: 25.1; 41.4; 43.2; 55.4; 114.1 (2C); 122.6 (2C); 122.7; 127.7 (2C); 129.6; 133.3; 134.8; 134.9; 142.0; 142.7; 159.5; 197.3; 198.1 (CO). Found, *m*/*z*: 305.1171 $[M+H]^+$. $C_{20}H_{17}O_3$. Calculated, *m*/*z*: 305.1172.

Synthesis of 2-aryl(alkenyl)-3-phenyl-2,3,4,4a-tetrahydro-5*H*-indeno[1,2-*c*]pyridazin-5-ones 4a–f (General method). $Sc(OTf)_3$ (36 mg, 20 mol %) was added to a solution of cyclopropane **1a–f** (0.6 mmol) and phenylhydrazine (0.63 mmol, 1.05 equiv) in dry CH_2Cl_2 (0.08 M solution) in the presence of 4 Å molecular sieves. The reaction mixture was stirred until complete conversion of the starting cyclopropane (TLC control) at room temperature (unless indicated otherwise) under argon atmosphere. The mixture was poured into saturated aqueous $NaHCO_3$ (15 ml), and extracted with CH_2Cl_2 (3×8 ml). The organic layer was washed with saturated aqueous $NaHCO_3$ (3×8 ml) followed by H_2O (2×4 ml). The solvent was evaporated under reduced pressure, and the product was purified by column chromatography on silica gel, eluent petroleum ether – EtOAc, gradient from 10:1 to 4:1.

(3*RS*,4a*SR*)-2,3-Diphenyl-2,3,4,4a-tetrahydro-5*H*-indeno[1,2-*c*]pyridazin-5-one (4a). The reaction mixture was heated under reflux for 3 h. Yield 115 mg (57%), dark-yellow crystals, mp 162–163°C (decomp.), R_f 0.59 (petroleum ether – EtOAc, 4:1). IR spectrum, ν, cm^{-1}: 3060, 3035, 2945, 2870, 1715, 1590, 1495, 1455, 1380, 1285, 1255, 1135, 990, 865, 750, 695. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.08–2.10 (1H, m, CH_2); 2.74 (1H, ddd, ^2J = 12.6, ^3J = 5.7, ^3J = 2.0, CH_2); 2.90 (1H, dd, ^3J = 12.8, ^3J = 5.6, CH); 5.38 (1H, dd, ^3J = 5.0, ^3J = 2.0, CH); 6.89–6.93 (1H, m, H Ar); 7.24–7.29 (5H, m, H Ar); 7.33–7.38 (4H, m, H Ar); 7.44–7.46 (1H, m, H Ar); 7.71–7.74 (1H, m, H Ar); 7.78 (1H, d, ^3J = 7.7, H Ar); 8.05 (1H, d, ^3J = 7.8, H Ar). ^{13}C NMR spectrum, δ, ppm: 27.2 (CH_2); 39.6 (CH); 57.6 (CH); 114.3 (2CH); 120.9 (CH); 121.2 (CH); 123.6 (CH); 126.3 (2CH); 127.9 (CH); 129.2 (5CH); 135.6 (CH); 137.2 (C); 140.0 (C); 140.7 (2C); 146.4 (C); 146.8 (C); 200.8 (CO). Found, *m*/*z*: 339.1487 $[M+H]^+$. $C_{23}H_{19}N_2O$. Calculated, *m*/*z*: 339.1492.

(3*RS*,4a*SR*)-3-(4-Methylphenyl)-2-phenyl-2,3,4,4a-tetrahydro-5*H*-indeno[1,2-*c*]pyridazin-5-one (4b). The reaction mixture was heated under reflux for 3 h. Yield 125 mg (59%), orange foam, R_f 0.67 (petroleum ether – EtOAc, 4:1). IR spectrum, ν, cm^{-1}: 3060, 3030, 2955, 2930, 2835, 1715, 1595, 1510, 1495, 1375, 1290, 1250, 1175, 1130, 1030, 990, 865, 750, 690. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.01–2.08 (1H, m, CH_2); 2.35 (3H, s, CH_3); 2.74 (1H, ddd, ^2J = 12.8, ^3J = 5.6, ^3J = 2.0, CH_2); 2.93 (1H, dd, ^3J = 12.8, ^3J = 5.7, CH); 5.37 (1H, dd, ^3J = 4.9, ^3J = 2.1, CH); 6.91–6.94 (1H, m, H Ar); 7.14–7.19 (4H, m, H Ar); 7.26–7.29 (2H, m, H Ar); 7.34–7.36 (2H, m, H Ar); 7.43–7.47 (1H, m, H Ar); 7.71–7.74 (1H, m, H Ar); 7.79 (1H, d, ^3J = 7.7, H Ar); 8.05 (1H, d, ^3J = 7.8, H Ar). ^{13}C NMR spectrum, δ, ppm: 21.2; 27.3; 39.7; 57.5; 114.3 (2C); 120.9; 121.2; 123.7; 126.2 (2C); 129.2 (3C); 129.9 (2C); 135.6; 137.2; 137.6; 137.7; 140.0; 146.5; 146.9; 201.0. Found, *m*/*z*: 353.1645 $[M+H]^+$. $C_{24}H_{21}N_2O$. Calculated, *m*/*z*: 353.1648.

(3*RS*,4a*SR*)-3-(4-Methoxyphenyl)-2-phenyl-2,3,4,4a-tetrahydro-5*H*-indeno[1,2-*c*]pyridazin-5-one (4c). The reaction mixture was stirred at room temperature for 50 min. Yield 150 mg (68%), orange foam, R_f 0.41 (petroleum ether – EtOAc, 4:1). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.01–2.08 (1H, m, CH_2); 2.70 (1H, ddd, ^2J = 12.6, ^3J = 5.6, ^3J = 2.0, CH_2); 2.93 (1H, dd, ^3J = 12.8, ^3J = 5.6, CH); 3.80 (3H, s, OCH_3); 5.34–5.37 (1H, m, CH); 6.91 (2H, d, ^3J = 8.7, H Ar); 6.92–6.95 (1H, m, H Ar); 7.18 (2H, d, ^3J = 8.7, H Ar); 7.28–7.31 (2H, m, H Ar); 7.35–7.37 (2H, m, H Ar); 7.43–7.47 (1H, m, H Ar); 7.71–7.74 (1H, m, H Ar); 7.80 (1H, d, ^3J = 7.7, H Ar); 8.05 (1H, d, ^3J = 7.8, H Ar). ^{13}C NMR spectrum, δ, ppm: 27.3; 39.6; 55.4; 57.0; 114.2 (2C); 114.6 (2C); 120.8; 121.1; 123.6; 127.3 (2C); 129.1 (3C); 132.4; 135.5; 137.2; 139.9; 146.4; 146.8; 159.3; 200.9 (CO). Found, *m*/*z*: 369.1595 $[M+H]^+$. $C_{24}H_{21}N_2O_2$. Calculated, *m*/*z*: 369.1598.

(3*RS*,4a*SR*)-3-(4-Fluorophenyl)-2-phenyl-2,3,4,4a-tetrahydro-5*H*-indeno[1,2-*c*]pyridazin-5-one (4d). The reaction mixture was heated under reflux for 5 h. Yield 103 mg (48%), orange foam, R_f 0.58 (petroleum ether – EtOAc, 4:1). IR spectrum, ν, cm^{-1}: 2995, 2935, 2835, 1715, 1590, 1495, 1455, 1415, 1375, 1330, 1290, 1235, 1125, 1005, 970, 750, 700. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.04–2.11 (1H, m, CH_2); 2.72 (1H, ddd, ^2J = 12.7, ^3J = 5.7, ^3J = 1.7, CH_2); 2.87 (1H, dd, ^3J = 12.9, ^3J = 5.7, CH); 5.37–5.40 (1H, m, CH); 6.92–6.97 (1H, m, H Ar); 7.04–7.09 (2H, m, H Ar); 7.22–7.34 (5H, m, H Ar); 7.44–7.46 (1H, m, H Ar); 7.71–7.75 (1H, m, H Ar); 7.78–7.81 (1H, m, H Ar); 7.80 (1H, d, ^3J = 7.7, H Ar); 8.05 (1H, d, ^3J = 7.8, H Ar). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 27.2; 39.4; 57.0; 114.2 (2C); 116.2 (2C, d, J_{CF} = 22.0); 121.0; 121.2; 123.7; 127.9 (2C, d, J_{CF} = 8.0); 129.2 (2C); 129.3; 135.7; 136.4; 137.2; 140.0; 146.2; 146.7; 163.3 (C, d, J_{CF} = 254.0); 200.6. Found, *m*/*z*: 357.1401 $[M+H]^+$. $C_{23}H_{18}FN_2O$. Calculated, *m*/*z*: 357.1398.

3-(3,4,5-Trimethoxyphenyl)-2-phenyl-2,3,4,4a-tetrahydro-5*H*-indeno[1,2-*c*]pyridazin-5-one (4e). The reaction mixture was stirred at room temperature for 1.5 h. Yield 157 mg (61%), orange foam, R_f 0.36 (petroleum ether – EtOAc, 4:1). IR spectrum, ν, cm^{-1}: 3070, 3055, 2950, 1705, 1595, 1510, 1420, 1375, 1335, 1235, 1160, 1040, 990, 835, 735, 670. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.99–2.07 (1H, m, CH_2); 2.74 (1H, ddd, ^2J = 12.5, ^3J = 5.6, ^3J = 1.7, CH_2); 2.97 (1H, dd, ^3J = 12.8, ^3J = 5.6, CH); 3.82 (6H, s, $2OCH_3$); 3.85 (3H, s, OCH_3); 5.31 (1H, dd, ^3J = 5.0, ^3J = 1.7, CH); 6.46 (2H, s, H Ar); 6.93–6.97 (1H, m, H Ar); 7.27–7.31 (2H, m, H Ar); 7.33–7.36 (2H, m, H Ar); 7.44–7.48 (1H, m, H Ar); 7.71–7.75 (1H, m, H Ar); 7.81 (1H, d,

^3J = 7.7, H Ar); 8.05 (1H, d, ^3J = 7.8, H Ar). ^{13}C NMR spectrum, δ, ppm: 27.3; 39.8; 56.4 (2C); 58.2; 61.0; 103.2 (2C); 114.6 (2C); 121.1; 121.2; 123.7; 129.2 (2C); 129.3; 135.7; 136.4; 137.2; 137.7; 140.2; 146.7 (2C); 154.0 (2C); 200.9. Found, *m*/*z*: 429.1812 $[M+H]^+$. $C_{26}H_{25}N_2O_4$. Calculated, *m*/*z*: 429.1809.

3-[2-(4-Methoxyphenyl)ethenyl]-2-phenyl-2,3,4,4a-tetrahydro-5*H*-indeno[1,2-*c*]pyridazin-5-one (4f). The reaction mixture was stirred at room temperature for 1 h. Yield 111 mg (47%), yellow-green foam, R_f 0.65 (petroleum ether – EtOAc, 4:1). IR spectrum, ν, cm^{-1}: 3060, 3030, 2930, 2835, 1710, 1595, 1510, 1495, 1470, 1375, 1285, 1250, 1175, 1135, 1035, 970, 820, 750, 690. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.82–1.90 (1H, m, CH_2); 2.64 (1H, ddd, ^2J = 12.7, ^3J = 5.8, ^3J = 1.8, CH_2); 3.28 (1H, dd, ^3J = 12.8, ^3J = 5.8, CH); 3.80 (3H, s, OCH_3); 4.93–4.97 (1H, m, CH); 6.12 (1H, dd, ^3J = 15.9, ^3J = 3.8, CH=); 6.38 (1H, dd, ^3J = 15.9, ^4J = 1.3, CH=); 6.84 (2H, d, ^3J = 8.8, H Ar); 6.97–7.00 (1H, m, H Ar); 7.29 (2H, d, ^3J = 8.8, H Ar); 7.35–7.38 (2H, m, H Ar); 7.44–7.50 (3H, m, H Ar); 7.70–7.73 (1H, m, H Ar); 7.81 (1H, d, ^3J = 7.7, H Ar); 8.02 (1H, d, ^3J = 7.8, H Ar). ^{13}C NMR spectrum, δ, ppm: 24.4; 40.1; 55.4; 55.5; 114.1 (2C); 114.3 (2C); 120.8; 121.1; 123.6; 124.2; 127.9 (2C); 128.7; 129.1; 129.2 (2C); 132.1; 135.5; 137.1; 139.7; 146.6; 146.7; 159.6; 201.0. Found, *m*/*z*: 395.1755 $[M+H]^+$. $C_{26}H_{23}N_2O_2$. Calculated, *m*/*z*: 395.1754.

X-ray structural analysis of compounds 1a and 4a. Crystals of compounds **1a** and **4a** suitable for X-ray analysis were obtained from petroleum ether – EtOAc solutions by slow evaporation of the solvent at room temperature. Analysis was performed on a STOE STADIVARI PILATUS-100K diffractometer, acquired within the framework of the program for the development of Moscow State University. The structures were solved by the direct method. All calculations were done using SHELXT and SHELXL-15 program sets.[23] Tables of atomic coordinates, bond lengths, valence and torsion angles, and anisotropic temperature parameters for compounds **1a** and **4a** were deposited at the Cambridge Crystallographic Data Center (deposits CCDC 1581845 and CCDC 1891023, respectively).

Supplementary information file containing ^{1}H and ^{13}C NMR data for compounds **1e**,**f** and **4a**–**f**, X-ray structural analysis data for compounds **1a** and **4a**, analysis of stereochemistry data for compounds **4a**–**f**, as well as quantum-chemical calculations results for compound **4a** and its isomers **4a'** and **4a''** using the HF/6-311G** method, is available at the journal website at http://link.springer.com/journal/10593.

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