DOI 10.1007/s10593-018-2193-2

Chemistry of Heterocyclic Compounds **2017**, *53*(11), 1192–1198

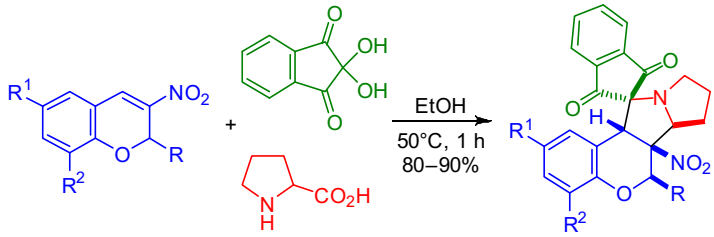
2-Substituted 3-nitro-2*H*-chromenes in reaction with azomethine ylide derived from ninhydrin and proline: regio- and stereoselective synthesis of spiro[chromeno[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-diones

Vladislav Yu. Korotaev[1]*, Igor B. Kutyashev[1], Alexey Yu. Barkov[1], Vyacheslav Ya. Sosnovskikh[1]

[1] *Institute of Natural Sciences and Mathematics, Ural Federal University named after the first President of Russia B. N. Yeltsin, 51 Lenina St., Yekaterinburg 620000, Russia; e-mail: korotaev.vladislav@urfu.ru*

Translated from Khimiya Geterotsiklicheskikh Soedinenii, 2017, *53*(11), 1192–1198

Submitted August 1, 2017
Accepted October 11, 2017



R = CF_3, Ph; R^1, R^2 = H, Me, MeO, EtO, Cl, Br, NO_2

Regio- and stereoselective 1,3-dipolar cycloaddition of stabilized azomethine ylides, generated *in situ* from ninhydrin and proline, occurred at the double bond activated by nitro group in 3-nitro-2-(trifluoromethyl)- and 3-nitro-2-phenyl-2*H*-chromenes upon heating in ethanol. This reaction produced high yields of spiro[chromeno[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-diones. The structure of the obtained products was confirmed by the method of X-ray crystallography.

Keywords: 3-nitro-2*H*-chromenes, spiro[chromeno[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-diones, stabilized azomethine ylides, 1,3-dipolar cycloaddition.

Fused ring systems containing chromene and chromane (3,4-dihydro-2*H*-1-benzopyran) motifs are often found in natural compounds, as well are included in biologically active synthetic molecules.[1] The notable biological activity of these compounds is primarily related to the simultaneous presence of several pharmacophoric fragments in one fused heterocyclic system. In particular, benzopyran **1** containing Δ^3-annulated pyrrolidine ring is an antagonist of 5-HT_{2C} receptors showing selectivity with regard to 5-HT_{2A} receptors,[2a] while its structural analog **2** is selective toward α1A and α1B adrenergic receptors, and has been proposed as a promising pharmaceutical agent for the treatment of benign prostatic hyperplasia[2b] (Fig. 1).

One of the most effective direct methods for the synthesis of pyrrolidines and pyrrolizidines, which has received an increasing attention from researchers over the recent years, relies on 1,3-dipolar cycloaddition of azomethine ylides at alkene double bonds.[3] Suitable examples of alkenes include 3-nitro-2*H*-chromenes that contain a reactive β-nitrostyrene moiety. The reactions of nitrochromenes with unstabilized and stabilized azomethine ylides derived from aldehydes and α-amino acids or their esters have been studied in considerable detail, resulting in the preparation of a broad range of chromane derivatives fused with pyrrolidine or pyrrolizidine rings.[4] However, their reactions with ylides of polycarbonyl compounds have been little studied: only two brief reports describe [3+2] addition of ylides derived from isatin and acenaphthenequinone to 2-substituted 3-nitro-2*H*-chromenes.[5]

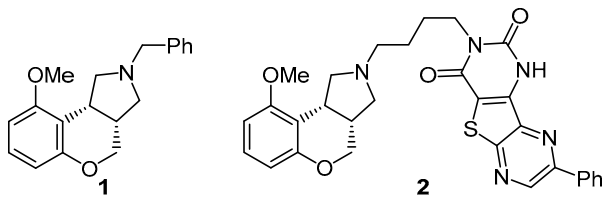


Figure 1. Biologically active chromeno[3,4-*c*]pyrrolidines.

The reactions of nitrochromenes with ylides prepared from ninhydrin have not been previously examined. At the same time, it has been reported that the azomethine ylide derived from ninhydrin and proline added regio- and stereoselectively to β-nitrostyrenes by attacking the electrophilic α-carbon atom of styrene with its more substituted part.[6] These reactions provided high yields of the respective *endo*-spirocycloadducts, the molecules of which contained pyrrolizidine ring along with the pharmacophoric indane-1,3-dione moiety.[6,7]

In a continuation of our studies aimed at the development of new methods for Δ^3-annulation of 3-nitro-2-(trihalomethyl)-2*H*-chromenes,[8] in the current work we studied a three-component reaction involving 2-substituted 3-nitro-2*H*-chromenes, ninhydrin, and proline, proposed a single-step method for the preparation of previously undescribed spiro[chromeno[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-diones, and studied their behavior in $CHCl_3$ and DMSO solutions.

It was found that the [3+2] cycloaddition of azomethine ylide, generated *in situ* from ninhydrin and proline, at the double bond of 3-nitro-2-(trifluoromethyl)-2*H*-chromenes **3a–i** in ethanol at 50°C over 1 h produced *endo*-spiro[chromeno[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-diones **4a–i** in 80–90% yields. The formation of regioisomeric adducts **4'a–i** did not occur due to the unfavorable dipole-dipole interaction arising between the C=O and NO_2 groups in the transition state[6] (Scheme 1, Table 1).

As shown in Table 1, the yields of products **4a–i** were little affected by the electron donor-acceptor properties of the substituents R^1 and R^2. When using other solvents (benzene, methanol, 2-propanol) in the reaction with chromene **3a**, the yields of adduct **4a** were lower by 10–30%.

3-Nitro-2-phenyl-2*H*-chromenes **3j–l** reacted with azomethine ylide obtained from ninhydrin and proline under analogous conditions, forming spirocycloadducts **4j–l** with the same regio- and stereospecificity (Scheme 1, Table 1). Again, the high yields of compounds **4j–l** (84–90%) were not affected by the nature of substituents in the starting chromenes.

The regio- and stereochemistry of products **4a–l** was confirmed by X-ray structural analysis of compound **4a** (Fig. 2). As shown in Figure 2, cycloadduct **4a** was indeed the regioisomer formed by addition of the C-2 atom of azomethine ylide at the more electrophilic C-4 atom of chromene. The trifluoromethyl substituent, nitro group, and the hydrogen atom at the C-11a position were in a *cis* configuration, while the hydrogen atom at the C-6b position was in a transoid orientation. The pyran ring had a half-chair conformation, while the five-membered ring annulated to it, as well as the next five-membered ring of the pyrrolizidine system assumed twist and envelope conformations, respectively.

Since the most favorable conformation for 2-substituted 3-nitro-2*H*-chromenes is half-chair with a pseudoaxial orientation of substituent,[9] the attack by azomethine ylide at the double bond of chromenes **3a–l** occurred from the side of pseudoequatorial 2-CH hydrogen atom (Scheme 1). As a result, the nitro group and substituent R in

Scheme 1

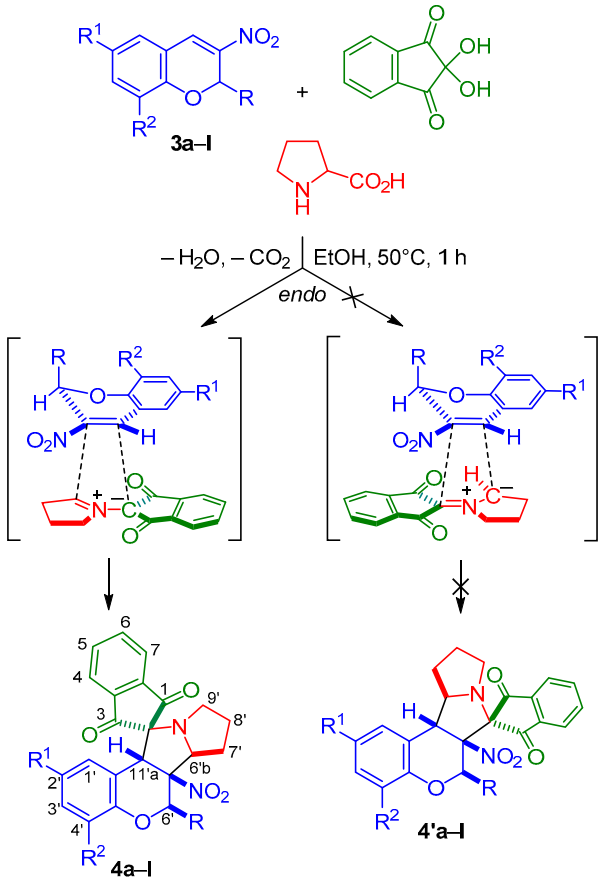


Table 1. Yields of chromeno[3,4-*a*]pyrrolizidines **4a–l**

Adduct	R	R^1	R^2	Yield, %	Adduct	R	R^1	R^2	Yield, %
4a	CF_3	H	H	83	**4g**	CF_3	Br	Br	90
4b	CF_3	Me	H	86	**4h**	CF_3	NO_2	H	87
4c	CF_3	MeO	H	80	**4i**	CF_3	NO_2	NO_2	89
4d	CF_3	H	EtO	80	**4j**	Ph	H	H	88
4e	CF_3	Cl	H	83	**4k**	Ph	MeO	H	84
4f	CF_3	Br	H	83	**4l**	Ph	Br	H	90

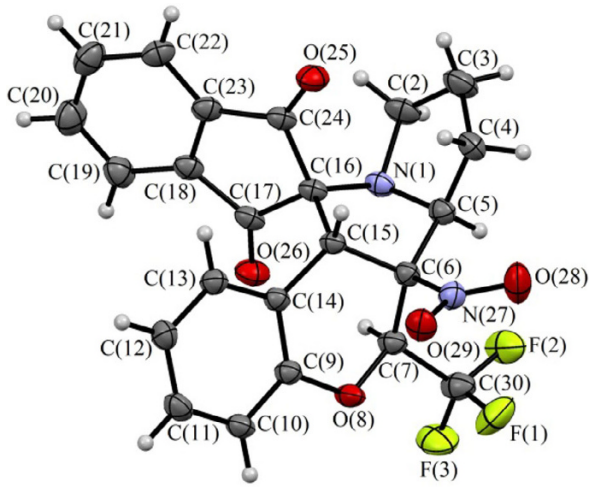


Figure 2. The molecular structure of compound **4a** with atoms represented by thermal vibration ellipsoids of 30% probability.

chromenopyrrolizidines **4a–l** were found in a *cis* relationship to each other, which is characteristic for the majority of adducts obtained by 1,3-dipolar cycloaddition involving 2-monosubstituted 3-nitro-2*H*-chromenes.[4,5,10]

^{1}H NMR spectra of compounds **4a–l** in $CDCl_3$ solution contained a characteristic singlet signal of the 1a-CH proton signal in the range of 4.68–5.12 ppm and a triplet or double doublet of the pyrrolizidine 6b-CH proton at the range of 4.04–4.60 ppm. The signal of the 6-CH proton appeared as a quartet at 5.78–6.22 ppm with spin-spin coupling constant $^3J_{HF}$ = 5.5–6.2 Hz in spectra of compounds **4a–i** or a singlet at 6.34–6.46 ppm in the spectra of compounds **4j–l**. The signal of trifluoromethyl group, which was bonded to an sp^3-hybridized carbon atom, appeared in ^{19}F NMR spectra of 6-CF_3-chromenopyrrolizidines **4a–i** as a doublet in the range of 91.7–93.7 ppm with spin-spin coupling constant $^3J_{FH}$ = 5.5–6.2 Hz. ^{13}C NMR spectra of compounds **4a–i** featured quartet signals of CF_3 group and C-6 carbon atom in the ranges of 121.6–122.8 and 75.3–75.8 ppm, respectively, with spin-spin coupling constants $^1J_{CF}$ = 280.3–286.7 and $^2J_{CF}$ = 33.1–34.3 Hz. IR spectra of products **4a–l** contained absorption bands due to the stretching vibrations of carbonyl group (1701–1709 cm^{-1}) and NO_2 group (1531–1554, 1339–1359 cm^{-1}).

In contrast to 6-phenylchromenopyrrolizidines **4j–l**, which remain stable also in DMSO-d_6 solution, the 6-trifluoromethyl-substituted adducts **4a–i** were unstable in this solvent and existed in equilibrium with the respective starting chromene **3** and azomethine ylide **5** (Scheme 2). Indeed, the dissolution of these compounds in DMSO-d_6 was immediately followed by the appearance of two new sets of ^{1}H NMR signals besides those of products **4a–i**, which were assigned to chromenes **3a–i** and azomethine ylide **5**[11] in the ratio of **3**:**5** = 1:1. The equilibrium compositions of mixtures containing compounds **3a–i**, **4a–i**, and **5** in DMSO-d_6 solution at 22°C are given in Table 2.

In conclusion, it should be noted that sterically hindered 3-nitro-2-phenyl-2-(trifluoromethyl)-2*H*-chromenes,[12] representing hybrid structures of chromenes **3a–l**, did not react with azomethine ylide **5** due to the steric hindrance arising in transition state between the bulky substituents at position 2 of chromene and the 1,3-indanedione moiety of ylide. Spirocycloadducts also could not be obtained in a reaction involving 2-CCl_3 analogs[13a] of nitrochromenes **3a–i**, with a high degree of resinification occurring in all of the cases. This was probably associated with the elimination of HCl molecule from 3-nitro-2-(trichloromethyl)-2*H*-chromenes by the action of basic azomethine ylide **5**, followed by the formation of unstable 2-(dichloromethylidene)chromenes. A similar process was observed by us upon treatment of 2-CCl_3-nitrochromenes with sodium azide.[8e]

Thus, 3-nitro-2-(trifluoromethyl)- and 3-nitro-2-phenyl-2*H*-chromenes reacted with azomethine ylide obtained from ninhydrin and proline, and the reaction proceeded as easily as the analogous reaction with β-nitrostyrenes. In contrast to 6-Ph-spirocycloadducts, the 6-CF_3-substituted products were unstable in DMSO solution. The molecules of the obtained compounds contained a combination of three pharmacophoric moieties and clearly should be of interest to researchers in the field of medicinal chemistry.

Scheme 2

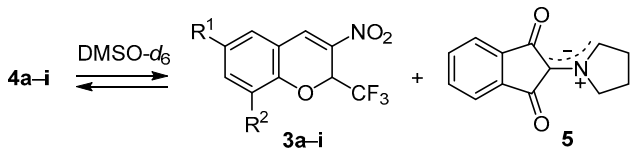


Table 2. The equilibrium **4a–i** ⇌ **3a–i** + **5** in DMSO-d_6 solution

The composition of mixture	Abundance of components, mol %		
	4	**3**	**5**
4a + **3a** + **5**	26	37	37
4b + **3b** + **5**	24	38	38
4c + **3c** + **5**	34	33	33
4d + **3d** + **5**	26	37	37
4e + **3e** + **5**	32	34	34
4f + **3f** + **5**	32	34	34
4g + **3g** + **5**	38	31	31
4h + **3h** + **5**	26	37	37
4i + **3i** + **5**	40	30	30

Experimental

IR spectra were recorded on a Bruker Alpha spectrometer equipped with an ATR accessory (ZnSe crystal). ^{1}H and ^{19}F NMR spectra were acquired on Bruker DRX-400 (400 and 376 MHz, respectively) and Bruker Avance 500 (500 and 471 MHz, respectively) spectrometers in $CDCl_3$ or DMSO-d_6, using TMS and C_6F_6 as internal standards. ^{13}C NMR spectra were acquired on a Bruker Avance-500 spectrometer (126 MHz) in $CDCl_3$ solution, using residual solvent signal (77.0 ppm) as internal standard. High-resolution mass spectra with electrospray ionization were recorded on a Waters Xevo QTof instrument. Elemental analysis was performed on an automatic PE 2400 elemental analyzer. Melting points were determined on an SMP40 apparatus.

The starting nitrochromenes **3a–l** were obtained according to previously published procedures.[13]

Preparation of spiro[chromeno[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-diones **4a–l** (General method). A mixture of nitrochromene **3a–l** (1.0 mmol), ninhydrin (0.18 g, 1.0 mmol), and proline (0.17 g, 1.5 mmol) in ethanol (5 ml) was stirred at 50°C for 1 h. The reaction mixture was then cooled to room temperature, the precipitate was filtered off, washed first with ethanol (3×3 ml) and then with water (3×1 ml), and dried at 60°C. Products **4a–l** were isolated as greenish-yellow powders.

(6*S,6a*S**,6b*S**,11a*R**)-6a-Nitro-6-trifluoromethyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-dione (4a)**. Yield 0.38 g (83%), mp 162–163°C (decomp.). IR spectrum, ν, cm^{-1}: 1705, 1554, 1490, 1459, 1397, 1370, 1354, 1329. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.84–3.33 (6H, m, $3CH_2$); 4.60 (1H, t, *J* = 7.3, 6b-CH); 5.12 (1H, s, 11a-CH); 5.84 (1H, q, *J* = 6.2, 6-CH); 6.34 (1H, d, *J* = 7.7, H-1); 6.64 (1H, t, *J* = 6.4, H-2); 7.03 (1H, d, *J* = 8.2, H-4); 7.12 (1H, t, *J* = 7.8, H-3); 7.83 (1H, d, *J* = 7.6, H-4'(7')); 7.93 (1H, t, *J* = 7.5, H-5'(6')); 7.99 (1H, t, *J* = 7.5, H-6'(5')); 8.17 (1H, d, *J* = 7.6, H-7'(4')). ^{1}H NMR spectrum

(500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.69–2.85 (6H, m, $3CH_2$); 4.26 (1H, br. t, *J* = 7.9, 6b-CH); 4.86 (1H, s, 11a-CH); 6.01 (1H, q, *J* = 6.2, 6-CH); 6.31 (1H, d, *J* = 7.6, H-1); 6.69 (1H, t, *J* = 7.6, H-3); 7.05 (1H, d, *J* = 8.1, H-4); 7.16 (1H, br. t, *J* = 7.5, H-2); 7.81 (1H, d, *J* = 7.6, H-4'(7')); 8.05 (1H, t, *J* = 7.5, H-5'(6')); 8.14 (1H, t, *J* = 7.5, H-6'(5')); 8.22 (1H, d, *J* = 7.6, H-7'(4')). ^{19}F NMR spectrum (471 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 93.6 (d, *J* = 6.2, CF_3). ^{19}F NMR spectrum (471 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 93.4 (d, *J* = 6.2, CF_3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 24.8; 29.1; 48.1; 50.0; 69.5; 74.6; 75.6 (q, *J* = 33.4, C-6); 93.1; 117.7; 120.0; 122.7; 122.8 (q, *J* = 281.5, CF_3); 123.8; 124.3; 126.6; 129.1; 131.8; 136.7; 137.2; 141.8; 151.9; 197.6; 197.7. Found, %: C 59.31; H 3.83; N 6.05. $C_{23}H_{17}F_3N_2O_5 \cdot 0.33H_2O$. Calculated, %: C 59.49; H 3.83; N 6.03.

(6*S,6a*S**,6b*S**,11a*R**)-2-Methyl-6a-nitro-6-trifluoromethyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno-[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-dione (4b)**. Yield 0.41 g (86%), mp 150–151°C (decomp.). IR spectrum, ν, cm^{-1}: 1705, 1551, 1504, 1399, 1369, 1354, 1333. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.82–3.29 (6H, m, $3CH_2$); 1.86 (3H, s, CH_3); 4.57 (1H, t, *J* = 7.3, 6b-CH); 5.04 (1H, s, 11a-CH); 5.79 (1H, q, *J* = 6.2, 6-CH); 6.07 (1H, br. s, H-1); 6.87–6.92 (2H, m, H-3,4); 7.86 (1H, d, *J* = 7.6, H-4'(7')); 7.92 (1H, td, *J* = 7.5, *J* = 1.0, H-5'(6')); 7.99 (1H, td, *J* = 7.5, *J* = 1.0, H-6'(5')); 8.18 (1H, d, *J* = 7.6, H-7'(4')). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.68–2.87 (6H, m, $3CH_2$); 1.79 (3H, s, CH_3); 4.26 (1H, dd, *J* = 8.9, *J* = 6.7, 6b-CH); 4.77 (1H, s, 11a-CH); 5.95 (1H, q, *J* = 6.2, 6-CH); 6.01 (1H, br. s, H-1); 6.92 (1H, d, *J* = 8.4, H-4); 6.94 (1H, br. d, *J* = 8.4, H-3); 7.79 (1H, d, *J* = 7.6, H-4'(7')); 8.06 (1H, t, *J* = 7.5, H-5'(6')); 8.14 (1H, t, *J* = 7.5, H-6'(5')); 8.23 (1H, d, *J* = 7.6, H-7'(4')). ^{19}F NMR spectrum (471 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 93.6 (d, *J* = 6.2, CF_3). ^{19}F NMR spectrum (376 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 93.4 (d, *J* = 6.2, CF_3). ^{13}C NMR spectrum, δ, ppm, (*J*, Hz): 20.3; 24.8; 29.0; 48.2; 50.0; 69.4; 75.1; 75.5 (q, *J* = 33.1, C-6'); 92.9; 117.3; 120.0; 122.6; 122.7 (q, *J* = 281.0, CF_3); 123.8; 124.3; 126.9; 130.0; 132.1; 136.7; 137.2; 141.7; 149.8; 198.2; 198.4. Found, *m/z*: 473.1320 $[M+H]^+$. $C_{24}H_{20}F_3N_2O_5$. Calculated, *m/z*: 473.1319.

(6*S,6a*S**,6b*S**,11a*R**)-2-Methoxy-6a-nitro-6-trifluoromethyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno-[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-dione (4c)**. Yield 0.39 g (80%), mp 175–176°C (decomp.). IR spectrum, ν, cm^{-1}: 1703, 1553, 1503, 1466, 1399, 1370, 1355, 1333. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.78–3.18 (6H, m, $3CH_2$); 3.27 (3H, s, CH_3O); 4.47 (1H, t, *J* = 7.2, 6b-CH); 5.02 (1H, s, 11a-CH); 5.77 (1H, d, *J* = 2.9, H-1); 5.78 (1H, q, *J* = 6.2, 6-CH); 6.65 (1H, dd, *J* = 9.0, *J* = 2.9, H-3); 6.94 (1H, d, *J* = 9.0, H-4); 7.86 (1H, d, *J* = 7.6, H-4'(7')); 7.92 (1H, td, *J* = 7.6, *J* = 1.0, H-5'(6')); 7.97 (1H, td, *J* = 7.6, *J* = 1.0, H-6'(5')); 8.16 (1H, d, *J* = 7.6, H-7'(4')). ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.68–2.86 (6H, m, $3CH_2$); 3.14 (3H, s, CH_3O); 4.25 (1H, dd, *J* = 8.8, *J* = 6.5, 6b-CH); 4.80 (1H, s, 11a-CH); 5.71 (1H, d, *J* = 2.9, H-1); 5.91 (1H, q, *J* = 6.2, 6-CH); 6.72 (1H, dd, *J* = 9.0, *J* = 2.9, H-3); 6.99 (1H, d, *J* = 9.0, H-4); 7.82 (1H, d, *J* = 7.6, H-4'(7')); 8.06 (1H, td, *J* = 7.6, *J* = 1.0, H-5'(6')); 8.14 (1H, td, *J* = 7.6, *J* = 1.0, H-6'(5')); 8.22 (1H, d, *J* = 7.6, H-7'(4')). ^{19}F NMR spectrum (471 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 93.2 (d, *J* = 6.1, CF_3). ^{19}F NMR spectrum (471 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 93.5 (d, *J* = 6.2, CF_3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 24.6; 28.7; 48.7; 50.1; 58.7; 69.5; 74.1; 75.9 (q, *J* = 33.4, C-6); 93.4; 110.8; 115.9; 118.6; 120.1; 122.7 (q, *J* = 281.3, CF_3); 123.9; 124.5; 131.8; 136.8; 137.5; 141.7; 142.0; 154.8; 197.1; 197.4. Found, *m/z*: 489.1267 $[M+H]^+$. $C_{24}H_{20}F_3N_2O_6$. Calculated, *m/z*: 489.1268.

(6*S,6a*S**,6b*S**,11a*R**)-4-Ethoxy-6a-nitro-6-trifluoromethyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno-[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-dione (4d)**. Yield 0.40 g (80%), mp 169–170°C (decomp.). IR spectrum, ν, cm^{-1}: 1708, 1553, 1390, 1359, 1337. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.40 (3H, t, *J* = 7.0, CH_3); 1.81–3.27 (6H, m, $3CH_2$); 4.01 (1H, dq, *J* = 10.6, *J* = 7.0, OCH_2); 4.03 (1H, dq, *J* = 10.6, *J* = 7.0, OCH_2); 4.54 (1H, t, *J* = 7.0, 6b-CH); 5.11 (1H, s, 11a-CH); 5.80 (1H, q, *J* = 6.2, 6-CH); 5.90 (1H, d, *J* = 7.8, H-1); 6.53 (1H, t, *J* = 7.9, H-2); 6.68 (1H, d, *J* = 8.0, H-3); 7.85 (1H, d, *J* = 7.6, H-4'(7')); 7.91 (1H, t, *J* = 7.5, H-5'(6')); 7.97 (1H, t, *J* = 7.5, H-6'(5')); 8.15 (1H, d, *J* = 7.6, H-7'(4')). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.31 (3H, t, *J* = 6.9, CH_3); 1.66–2.83 (6H, m, $3CH_2$); 4.09 (1H, dq, *J* = 9.8, *J* = 6.9, OC<u>H</u>H); 4.13 (1H, dq, *J* = 9.8, *J* = 6.9, OCH<u>H</u>); 4.26 (1H, br. t, *J* = 7.8, 6b-CH); 4.84 (1H, s, 11a-CH); 5.84 (1H, d, *J* = 7.8, H-1); 5.94 (1H, q, *J* = 6.2, 6-CH); 6.60 (1H, t, *J* = 8.1, H-2); 6.84 (1H, d, *J* = 8.4, H-3); 7.83 (1H, d, *J* = 7.6, H-4'(7')); 8.05 (1H, t, *J* = 7.5, H-5'(6')); 8.14 (1H, t, *J* = 7.5, H-6'(5')); 8.22 (1H, d, *J* = 7.6, H-7'(4')). ^{19}F NMR spectrum (471 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 93.7 (d, *J* = 6.2, CF_3). ^{19}F NMR spectrum (376 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 93.8 (d, *J* = 6.2, CF_3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 14.7; 24.8; 28.9; 48.2; 49.9; 65.2; 69.5; 75.0; 75.3 (q, *J* = 33.7, C-6); 93.4; 113.7; 117.7; 118.1; 122.5; 122.8 (q, *J* = 280.3, CF_3); 123.9; 124.3; 136.6; 137.2; 141.7; 141.8; 142.4; 148.2; 198.0; 198.2. Found, *m/z*: 503.1423 $[M+H]^+$. $C_{25}H_{22}F_3N_2O_6$. Calculated, *m/z*: 503.1424.

(6*S,6a*S**,6b*S**,11a*R**)-2-Chloro-6a-nitro-6-trifluoromethyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno-[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-dione (4e)**. Yield 0.41 g (83%), mp 167–168°C (decomp.). IR spectrum, ν, cm^{-1}: 1701, 1552, 1486, 1382, 1353. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.79–3.15 (6H, m, $3CH_2$); 4.46 (1H, t, *J* = 7.3, 6b-CH); 4.96 (1H, s, 11a-CH); 5.87 (1H, q, *J* = 6.1, 6-CH); 6.29 (1H, d, *J* = 2.3, H-1); 6.97 (1H, d, *J* = 8.8, H-4); 7.07 (1H, dd, *J* = 8.8, *J* = 2.3, H-3); 7.88 (1H, d, *J* = 7.6, H-4'(7')); 7.95 (1H, td, *J* = 7.5, *J* = 1.0, H-5'(6')); 8.01 (1H, td, *J* = 7.5, *J* = 1.0, H-6'(5')); 8.18 (1H, d, *J* = 7.6, H-7'(4')). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.71–2.89 (6H, m, $3CH_2$); 4.23 (1H, dd, *J* = 9.2, *J* = 6.5, 6b-CH); 4.87 (1H, s, 11a-CH); 6.02 (1H, q, *J* = 6.1, 6-CH); 6.25 (1H, d, *J* = 2.6, H-1); 7.10 (1H, d, *J* = 8.8, H-4); 7.58 (1H, dd, *J* = 8.8, *J* = 2.6, H-3); 7.81 (1H, d, *J* = 7.6, H-4'(7')); 8.07 (1H, td, *J* = 7.5, *J* = 1.0, H-5'(6')); 8.16 (1H, td, *J* = 7.5, *J* = 1.0, H-6'(5')); 8.23 (1H,

d, J = 7.6, H-7'(4')). ^{19}F NMR spectrum (471 MHz, $CDCl_3$), δ, ppm (J, Hz): 93.0 (d, J = 6.1, CF_3). ^{19}F NMR spectrum (376 MHz, DMSO-d_6), δ, ppm (J, Hz): 92.9 (d, J = 6.1, CF_3). ^{13}C NMR spectrum, δ, ppm (J, Hz): 24.6; 28.9; 47.7; 50.1; 69.3; 74.4; 75.5 (q, J = 33.6, C-6); 92.2; 117.7; 117.8; 119.1; 122.5 (q, J = 281.6, CF_3); 124.2; 124.6; 126.3; 129.6; 137.2; 137.7; 141.6; 141.8; 150.5; 197.2; 197.3. Found, *m*/*z*: 493.0771 $[M+H]^+$. $C_{23}H_{17}ClF_3N_2O_5$. Calculated, *m*/*z*: 493.0773.

(6*S,6a*S**,6b*S**,11a*R**)-2-Bromo-6a-nitro-6-trifluoromethyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno-[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-dione (4f)**. Yield 0.45 g (83%), mp 152–153°C (decomp.). IR spectrum, ν, cm^{-1}: 1702, 1551, 1484, 1370, 1351, 1329. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.81–3.19 (6H, m, $3CH_2$); 4.49 (1H, t, J = 7.4, 6b-CH); 4.96 (1H, s, 11a-CH); 5.86 (1H, q, J = 6.0, 6-CH); 6.42 (1H, d, J = 2.2, H-1); 6.91 (1H, d, J = 8.8, H-4); 7.21 (1H, dd, J = 8.8, J = 2.2, H-3); 7.88 (1H, d, J = 7.6, H-4'(7')); 7.96 (1H, td, J = 7.5, J = 1.1, H-5'(6')); 8.01 (1H, td, J = 7.5, J = 1.1, H-6'(5')); 8.18 (1H, d, J = 7.6, H-7'(4')). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (J, Hz): 1.70–2.90 (6H, m, $3CH_2$); 4.22 (1H, br. t, J = 7.2, 6b-CH); 4.87 (1H, s, 11a-CH); 6.01 (1H, q, J = 6.1, 6'-CH); 6.36 (1H, br. s, H-1); 7.16 (1H, d, J = 8.6, H-4); 7.70 (1H, dd, J = 8.6, J = 2.2, H-3); 7.81 (1H, d, J = 7.6, H-4'(7')); 8.07 (1H, t, J = 7.5, H-5'(6')); 8.16 (1H, t, J = 7.5, H-6'(5')); 8.23 (1H, d, J = 7.6, H-7'(4')). ^{19}F NMR spectrum (471 MHz, $CDCl_3$), δ, ppm (J, Hz): 93.0 (d, J = 6.0, CF_3). ^{19}F NMR spectrum (376 MHz, DMSO-d_6), δ, ppm (J, Hz): 92.8 (d, J = 6.1, CF_3). ^{13}C NMR spectrum, δ, ppm, (J, Hz): 24.8; 29.2; 47.6; 50.1; 69.1; 75.1; 75.3 (q, J = 33.6, C-6); 91.9; 114.9; 118.6; 119.3; 122.5 (q, J = 281.6, CF_3); 124.0; 124.4; 129.4; 132.3; 137.0; 137.6; 141.6; 141.7; 150.9; 198.0; 198.1. Found, *m*/*z*: 537.0267 $[M+H]^+$. $C_{23}H_{17}BrF_3N_2O_5$. Calculated, *m*/*z*: 537.0267.

(6*S,6a*S**,6b*S**,11a*R**)-2,4-Dibromo-6a-nitro-6-trifluoromethyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-dione (4g)**. Yield 0.55 g (90%), mp 173–174°C (decomp.). IR spectrum, ν, cm^{-1}: 1701, 1554, 1408, 1355. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.77–3.05 (6H, m, $3CH_2$); 4.39 (1H, t, J = 7.5, 6b-CH); 4.92 (1H, s, 11a-CH); 5.92 (1H, q, J = 5.9, 6-CH); 6.37 (1H, d, J = 2.1, H-1); 7.49 (1H, d, J = 2.1, H-3); 7.88 (1H, d, J = 7.5, H-4'(7')); 7.96 (1H, dd, J = 7.5, J = 1.1, H-5'(6')); 8.01 (1H, dd, J = 7.5, J = 1.1, H-6'(5')); 8.17 (1H, d, J = 7.5, H-7'(4')). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (J, Hz): 1.72–2.91 (6H, m, $3CH_2$); 4.22 (1H, dd, J = 9.1, J = 6.3, 6b-CH); 4.96 (1H, s, 11a-CH); 6.08 (1H, q, J = 5.9, 6-CH); 6.39 (1H, d, J = 2.0, H-1); 7.84 (1H, d, J = 7.6, H-4'(7')); 7.76 (1H, d, J = 2.0, H-3); 8.07 (1H, t, J = 7.5, H-5'(6')); 8.16 (1H, t, J = 7.5, H-6'(5')); 8.22 (1H, d, J = 7.6, H-7'(4')). ^{19}F NMR spectrum (471 MHz, $CDCl_3$), δ, ppm (J, Hz): 92.7 (d, J = 5.9, CF_3). ^{19}F NMR spectrum (376 MHz, DMSO-d_6), δ, ppm (J, Hz): 92.6 (d, J = 5.9, CF_3). ^{13}C NMR spectrum, δ, ppm (J, Hz): 24.8; 29.3; 47.7; 49.9; 69.1; 74.5; 75.8 (q, J = 34.0, C-6); 91.9; 112.7; 114.7; 120.0; 122.3 (q, J = 287.6, CF_3); 124.0; 124.5; 128.5; 131.9; 135.3; 137.1; 137.6; 141.6; 148.2; 198.1; 198.3. Found, %: C 44.61; H 2.38; N 4.56. $C_{23}H_{15}Br_2F_3N_2O_5$. Calculated, %: C 44.83; H 2.45; N 4.55.

(6*S,6a*S**,6b*S**,11a*R**)-2,6a-Dinitro-6-trifluoromethyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno[3,4-*a*]-pyrrolizidine-11,2'-indene]-1',3'-dione (4h)**. Yield 0.44 g (87%), mp 147–148°C (decomp.). IR spectrum, ν, cm^{-1}: 1707, 1589, 1564, 1533, 1346, 1329. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.84–3.06 (6H, m, $3CH_2$); 4.43 (1H, t, J = 7.7, 6b-CH); 4.91 (1H, s, 11a-CH); 6.05 (1H, q, J = 5.8, 6-CH); 7.16 (1H, d, J = 9.1, H-4); 7.25 (1H, d, J = 2.1, H-1); 7.80 (1H, d, J = 7.7, H-4'(7')); 7.93 (1H, td, J = 7.6, J = 1.0, H-5'(6')); 8.00–8.05 (2H, m, H-6'(5'), H-3); 8.22 (1H, d, J = 7.7, H-7'(4')). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (J, Hz): 1.76–2.91 (6H, m, $3CH_2$); 4.23 (1H, dd, J = 9.5, J = 6.3, 6b-CH); 5.10 (1H, s, 11a-CH); 6.16 (1H, q, J = 5.7, 6-CH); 7.12 (1H, d, J = 2.3, H-1); 7.34 (1H, d, J = 9.1, H-4); 7.72 (1H, d, J = 7.8, H-4'(7')); 8.01 (1H, br. t, J = 7.8, H-5'(6')); 8.05 (1H, dd, J = 9.1, J = 2.3, H-3); 8.14 (1H, t, J = 7.8, H-6'(5')); 8.25 (1H, d, J = 7.7, H-7'(4')). ^{19}F NMR spectrum (471 MHz, $CDCl_3$), δ, ppm (J, Hz): 92.2 (d, J = 5.8, CF_3). ^{19}F NMR spectrum (471 MHz, DMSO-d_6), δ, ppm (J, Hz): 92.4 (d, J = 5.7, CF_3). ^{13}C NMR spectrum, δ, ppm (J, Hz): 24.8; 29.6; 47.4; 50.1; 69.0; 75.1; 75.4 (q, J = 34.2, C-6); 90.3; 117.5; 118.3; 120.3; 122.2 (q, J = 281.6, CF_3); 124.3; 125.1; 128.5; 131.9; 137.4; 137.8; 141.5; 141.7; 142.4; 198.2; 198.4. Found, %: C 54.73; H 3.15; N 8.31. $C_{23}H_{16}F_3N_3O_7$. Calculated, %: C 54.88; H 3.20; N 8.35.

(6*S,6a*S**,6b*S**,11a*R**)-2,4,6a-Trinitro-6-trifluoromethyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno-[3,4-*a*]pyrrolizidine-11,2'-indene]-1',3'-dione (4i)**. Yield 0.49 g (89%), mp 154–155°C (decomp.). IR spectrum, ν, cm^{-1}: 1706, 1538, 1401, 1339. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.80–2.98 (6H, m, $3CH_2$); 4.33 (1H, dd, J = 8.3, J = 7.3, 6b-CH); 4.90 (1H, s, 11a-CH); 6.22 (1H, q, J = 5.5, 6-CH); 7.46 (1H, d, J = 2.6, H-1); 7.84 (1H, d, J = 7.7, H-4'(7')); 7.96 (1H, td, J = 7.6, J = 1.0, H-5'(6')); 8.05 (1H, td, J = 7.6, J = 1.0, H-6'(5')); 8.22 (1H, d, J = 7.7, H-7'(4')); 8.67 (1H, d, J = 2.6, H-3). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (J, Hz): 1.77–3.07 (6H, m, $3CH_2$); 4.26 (1H, dd, J = 9.6, J = 6.3, 6b-CH); 5.32 (1H, s, 11a-CH); 6.28 (1H, q, J = 5.6, 6-CH); 7.43 (1H, d, J = 2.6, H-1); 7.79 (1H, d, J = 7.7, H-4'(7')); 8.71 (1H, d, J = 2.6, H-3); 8.07 (1H, t, J = 7.6, H-5'(6')); 8.16 (1H, t, J = 7.6, H-6'(5')); 8.26 (1H, d, J = 7.7, H-7'(4')). ^{19}F NMR spectrum (471 MHz, $CDCl_3$), δ, ppm (J, Hz): 91.7 (d, J = 5.5, CF_3). ^{19}F NMR spectrum (471 MHz, DMSO-d_6), δ, ppm (J, Hz): 92.4 (d, J = 5.6, CF_3). ^{13}C NMR spectrum, δ, ppm (J, Hz): 24.7; 29.7; 46.6; 50.1; 68.7; 74.9; 75.8 (q, J = 34.3, C-6'); 88.9; 121.4; 121.5; 121.6 (q, J = 282.0, CF_3); 124.4; 124.7; 125.8; 137.8; 138.1; 138.2; 140.7; 141.4; 141.6; 149.8; 197.7; 197.9. Found, %: C 50.35; H 2.76; N 10.04. $C_{23}H_{15}F_3N_4O_9$. Calculated, %: C 50.38; H 2.76; N 10.22.

(6*R,6a*S**,6b*S**,11a*R**)-6a-Nitro-6-phenyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno[3,4-*a*]-pyrrolizidine-11,2'-indene]-1',3'-dione (4j)**. Yield 0.41 g (88%), mp 163–164°C (decomp.). IR spectrum, ν, cm^{-1}:

1709, 1621, 1592, 1547, 1489, 1457, 1407, 1354, 1325. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.82–3.37 (6H, m, $3CH_2$); 4.34 (1H, dd, *J* = 9.1, *J* = 6.9, 6b-CH); 4.89 (1H, s, 11a-CH); 6.24 (1H, br. d, *J* = 7.4, H-1); 6.46 (1H, s, 6-CH); 6.57 (1H, td, *J* = 7.6, *J* = 1.1 H-2); 6.97 (1H, dd, *J* = 8.2, *J* = 1.1, H-4); 7.16 (1H, td, *J* = 7.7, *J* = 1.3 H-3); 7.45–7.49 (3H, m, H Ph); 7.59–7.64 (2H, m, H Ph); 7.88 (1H, br. d, *J* = 7.6, H-4'(7')); 7.94 (1H, td, *J* = 7.5, *J* = 1.0, H-5'(6')); 8.00 (1H, td, *J* = 7.5, *J* = 1.0, H-6'(5')); 8.17 (1H, br. d, *J* = 7.6, H-7'(4')). ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.62–2.95 (6H, m, $3CH_2$); 3.76 (1H, dd, *J* = 10.3, *J* = 5.8, 6b-CH); 4.62 (1H, s, 11a-CH); 6.21 (1H, dd, *J* = 7.9, *J* = 1.5, H-1); 6.49 (1H, s, 6-CH); 6.69 (1H, td, *J* = 7.6, *J* = 1.1 H-2); 6.94 (1H, dd, *J* = 8.2, *J* = 1.1, H-4); 7.16 (1H, td, *J* = 7.8, *J* = 1.5, H-3); 7.33–7.39 (2H, m, H Ph); 7.48–7.53 (3H, m, H Ph); 7.81 (1H, br. d, *J* = 7.6, H-4'(7')); 8.06 (1H, td, *J* = 7.5, *J* = 1.1, H-5'(6')); 8.14 (1H, td, *J* = 7.6, *J* = 1.0, H-6'(5')); 8.21 (1H, br. d, *J* = 7.7, H-7(4)). ^{13}C NMR spectrum, δ, ppm: 24.7; 29.9; 47.7; 50.8; 69.2; 76.0; 78.0; 93.6; 117.1; 117.7; 121.5; 123.7; 124.2; 127.2; 127.8 (2C); 128.2 (2C); 128.9; 129.4; 134.5; 136.7; 137.4; 141.5; 142.0; 154.0; 198.4; 200.0. Found, %: C 72.13; H 4.90; N 6.27. $C_{28}H_{22}N_2O_5$. Calculated, %: C 72.09; H 4.75; N 6.01.

(6*R,6a*S**,6b*S**,11a*R**)-2-Methoxy-6a-nitro-6-phenyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno[3,4-*a*]-pyrrolizidine-11,2'-indene]-1',3'-dione (4k)**. Yield 0.42 g (84%), mp 179–180°C (decomp.). IR spectrum, ν, cm^{-1}: 1708, 1622, 1590, 1539, 1501, 1456, 1408, 1353, 1325. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.88–3.48 (6H, m, $3CH_2$); 3.24 (3H, s, CH_3O); 4.50 (1H, br. t, *J* = 7.7, 6b-CH); 4.91 (1H, s, 11a-CH); 5.71 (1H, d, *J* = 2.9, H-1); 6.34 (1H, s, 6-CH); 6.67 (1H, dd, *J* = 9.0, *J* = 2.9, H-3); 6.90 (1H, d, *J* = 9.0, H-4); 7.45–7.49 (3H, m, H Ph); 7.61–7.66 (2H, m, H Ph); 7.93 (1H, br. d, *J* = 7.3, H-4'(7')); 7.97 (1H, td, *J* = 7.3, *J* = 1.1, H-5'(6')); 8.01 (1H, td, *J* = 7.3, *J* = 1.4, H-6'(5')); 8.19 (1H, br. d, *J* = 7.4, H-7'(4')). ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.62–2.95 (6H, m, $3CH_2$); 3.09 (3H, s, CH_3O); 3.75 (1H, dd, *J* = 10.4, *J* = 5.8, 6b-CH); 4.56 (1H, s, 11a-CH); 5.64 (1H, d, *J* = 2.9, H-1); 6.37 (1H, s, 6-CH); 6.67 (1H, dd, *J* = 8.9, *J* = 2.9 H-3); 6.87 (1H, d, *J* = 8.9, H-4); 7.32–7.38 (2H, m, H Ph); 7.47–7.52 (3H, m, H Ph); 7.83 (1H, br. d, *J* = 7.6, H-4'(7')); 8.07 (1H, td, *J* = 7.5, *J* = 1.1, H-5(6)); 8.14 (1H, td, *J* = 7.6, *J* = 1.0, H-6(5)); 8.21 (1H, br. d, *J* = 7.7, H-7(4)). ^{13}C NMR spectrum, δ, ppm: 24.7; 29.8; 48.3; 50.9; 55.1; 69.2; 75.7; 78.2; 93.8; 111.3; 115.7; 118.7; 123.7; 124.4; 127.8 (2C); 128.2 (2C); 129.4; 131.7; 134.5; 136.7; 137.5; 141.4; 142.2; 148.1; 153.8; 197.7; 199.6. Found, %: C 70.17; H 5.00; N 5.80. $C_{29}H_{24}N_2O_6$. Calculated, %: C 70.15; H 4.87; N 5.64.

(6*R,6a*S**,6b*S**,11a*R**)-2-Bromo-6a-nitro-6-phenyl-6a,6b,7,8,9,11a-hexahydro-6*H*-spiro[chromeno[3,4-*a*]-pyrrolizidine-11,2'-indene]-1',3'-dione (4l)**. Yield 0.49 g (90%), mp 194–195°C (decomp.). IR spectrum, ν, cm^{-1}: 1707, 1590, 1545, 1481, 1456, 1410, 1353, 1330. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.71–3.19 (6H, m, $3CH_2$); 4.04 (1H, dd, *J* = 10.4, *J* = 6.1, 6b-CH); 4.68 (1H, s, 11a-CH); 6.28 (1H, d, *J* = 2.3, H-1); 6.46 (1H, s, 6-CH); 6.86 (1H, d, *J* = 8.7, H-4); 7.18 (1H, dd, *J* = 8.7, *J* = 2.3, H-3); 7.43–7.49 (3H, m, H Ph); 7.50–7.55 (2H, m, H Ph); 7.87 (1H, br. d, *J* = 7.5, H-4'(7')); 7.97 (1H, td, *J* = 7.5, *J* = 1.0, H-5'(6')); 8.01 (1H, td, *J* = 7.5, *J* = 1.0, H-6'(5')); 8.18 (1H, br. d, *J* = 7.5, H-7'(4')). ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.63–2.96 (6H, m, $3CH_2$); 3.74 (1H, dd, *J* = 10.5, 5.7, 6b-CH); 4.65 (1H, s, 11a-CH); 6.28 (1H, d, *J* = 2.4, H-1); 6.44 (1H, s, 6-CH); 6.93 (1H, d, *J* = 8.7, H-4); 7.16 (1H, dd, *J* = 8.7, *J* = 2.4, H-3); 7.32–7.37 (2H, m, H Ph); 7.47–7.53 (3H, m, H Ph); 7.84 (1H, br. d, *J* = 7.6, H-4'(7')); 8.09 (1H, td, *J* = 7.5, *J* = 1.0, H-5'(6')); 8.16 (1H, td, *J* = 7.6, *J* = 1.0, H-6'(5')); 8.22 (1H, br. d, *J* = 7.6, H-7'(4')). ^{13}C NMR spectrum, δ, ppm: 24.8; 30.0; 47.5; 50.7; 69.0; 76.4; 78.2; 93.0; 113.4; 119.4; 119.5; 123.8; 124.2; 127.8 (2C); 128.3 (2C); 129.5; 130.1; 131.9; 134.1; 136.8; 137.6; 141.4; 141.9; 153.2; 198.7; 200.2. Found, %: C 61.53; H 3.88; N 5.34. $C_{28}H_{21}BrN_2O_5$. Calculated, %: C 61.66; H 3.88; N 5.14.

X-ray structural study of compound 4a was performed at 22°C on an Xcalibur diffractometer with an Eos CCD detector according to standard procedure (MoKα radiation, graphite monochromator, ω-scanning, $2\theta_{max}$ 56.4°. Crystals suitable for X-ray structural analysis were obtained by slowly evaporating a chloroform solution of compound **4a**. The structure of compound **4a** was solved by direct method using the SHELX97 software suite.[14] The positions of all non-hydrogen atoms were independently refined in anisotropic approximation, the hydrogen atoms were placed in geometrically calculated positions and included in the refinement according to the "rider" model with dependent temperature parameters. The complete X-ray structural dataset for compound **4a** was deposited at the Cambridge Crystallographic Data Center (deposit CCDC 1565370).

The work was performed with financial support from the Russian Science Foundation (*project 17-73-20070*).

References

1. (a) *The Chemistry of Heterocyclic Compounds: Chromans and Tocopherols*; Ellis, G. P.; Lockhart, I. M., Eds.; John Wiley & Sons: New York, 1981, Vol. 36. (b) Goel, A.; Ram, V. J. *Tetrahedron* **2009**, *65*, 7865. (c) Costa, M.; Dias, T. A.; Brito, A.; Proença, F. *Eur. J. Med. Chem.* **2016**, *123*, 487. (d) Unangst, P. C.; Capiris, T.; Connor, D. T.; Heffner, T. G.; MacKenzie, R. G.; Miller, S. R.; Pugsley, T. A.; Wise, L. D. *J. Med. Chem*. **1997**, *40*, 2688.
2. (a) Lavielle, G.; Dubuffet, T.; Millan, M.; Newman-Tancredi, A. US Patent 5663191; *Chem. Abstr.* **1996**, *124*, 261014. (b) Haight, A. R.; Bailey, A. E.; Baker, W. S.; Cain, M. H.; Copp, R. R.; DeMattei, J. A.; Ford, K. L.; Henry, R. F.; Hsu, M. C.; Keyes, R. F.; King, S. A.; McLaughlin, M. A.; Melcher, L. M.; Nadler, W. R.; Oliver, P. A.; Parekh, S. I.; Patel, H. H.; Seif, L. S.; Staeger, M. A.; Wayne, G. S.; Wittenberger, S. J.; Zhang, W. *Org. Process Res. Dev*. **2004**, *8*, 897.
3. (a) Döndas, H. A.; Retamosa, M. G.; Sansano, J. M. *Synthesis* **2017**, 2819. (b) Singh, M. S.; Chowdhury, S.; Koley, S. *Tetrahedron* **2016**, *72*, 1603.
4. (a) Nyerges, M.; Virányi, A.; Marth, G.; Dancsó, A.; Blaskó, G.; Tőke, L. *Synlett* **2004**, 2761. (b) Virányi, A.; Marth, G.;

Dancsó, A.; Blaskó, G.; Tőke, L.; Nyerges, M. *Tetrahedron* **2006**, *62*, 8720. (c) Korotaev, V. Yu.; Barkov, A. Yu.; Moshkin, V. S.; Matochkina, E. G.; Kodess, M. I.; Sosnovskikh, V. Ya. *Tetrahedron* **2013**, *69*, 8602. (d) Xie, J.-W.; Fan, L.-P.; Li, X.-S.; Xu, D.-C. *Org. Biomol. Chem.* **2010**, *8*, 2117.

5. (a) Rao, J. N. S.; Raghunathan, R. *Tetrahedron Lett.* **2013**, *54*, 6568. (b) Rao, J. N. S.; Raghunathan, R. *Tetrahedron Lett*. **2015**, *56*, 2276.
6. (a) Poornachandran, M.; Raghunathan, R. *Synth. Commun*. **2007**, *37*, 2507. (b) Barkov, A. Yu.; Zimnitskiy, N. S.; Korotaev, V. Yu.; Kutyashev, I. B.; Moshkin, V. S.; Sosnovskikh, V. Ya. *Chem. Heterocycl. Compd*. **2017**, *53*, 451. [*Khim. Geterotsikl. Soedin.* **2017**, *53*, 451.]
7. (a) Kathiravan, S.; Raghunathan, R.; Suresh, G.; Siva, G. V. *Med. Chem. Res*. **2012**, *21*, 3170. (b) Ajmi, N. S.; Ali, M. A.; Rusli, I.; Hasnah, O.; Kumar, R. S.; Tan, S. C.; Yeong, K. Y. WO Patent 2012099452 A1; *Chem. Abstr.* **2012**, *157*, 261573.
8. (a) Korotaev, V. Yu.; Sosnovskikh, V. Ya.; Barabanov, M. A.; Yasnova, E. S.; Ezhikova, M. A.; Kodess, M. I.; Slepukhin, P. A. *Tetrahedron* **2010**, *66*, 1404. (b) Korotaev, V. Yu.; Sosnovskikh, V. Ya.; Barkov, A. Yu.; Slepukhin, P. A.; Ezhikova, M. A.; Kodess, M. I.; Shklyaev, Yu. V. *Tetrahedron* **2011**, *67*, 8685. (c) Korotaev, V. Yu.; Barkov, A. Yu.; Sosnovskikh, V. Ya. *Tetrahedron* **2013**, *69*, 9642. (d) Korotaev, V. Yu.; Barkov, A. Yu.; Kutyashev, I. B.; Kotovich, I. V.; Ezhikova, M. A.; Kodess, M. I.; Sosnovskikh, V. Ya. *Tetrahedron* **2015**, *71*, 2658. (e) Korotaev, V. Yu.; Kutyashev, I. B.; Barkov, A. Yu.; Sosnovskikh, V. Ya. *Chem. Heterocycl. Compd*. **2017**, *53*, 597. [*Khim. Geterotsikl. Soedin.* **2017**, *53*, 597.]
9. (a) Kodukulla, R. P. K.; Hariharan, S.; Trivedi, G. K. *Tetrahedron* **1994**, *50*, 4623. (b) Yan, L.-J.; Zhang, S.-Y. *Acta Crystallogr*., *Sect. E: Crystallogr. Commun.* **2013**, *69*, o877.
10. Korotaev, V. Yu.; Sosnovskikh, V. Ya.; Barkov, A. Yu. *Russ. Chem. Rev*. **2013**, *82*, 1081. [*Usp. Khim.* **2013**, *82*, 1081.]
11. Kaupp, G.; Naimi-Jamal, M. R.; Schmeyers, J. *Chem.–Eur. J.* **2002**, *8*, 594.
12. Barkov, A. Yu.; Korotaev, V. Yu.; Kotovich, I. V.; Zimnitskiy, N. S.; Kutyashev, I. B.; Sosnovskikh, V. Ya. *Chem. Heterocycl. Compd*. **2016**, *52*, 814. [*Khim. Geterotsikl. Soedin.* **2016**, *52*, 814.]
13. (a) Korotaev, V. Yu.; Kutyashev, I. B.; Sosnovskikh, V. Ya. *Heteroat. Chem.* **2005**, *16*, 492. (b) Sakakibara, T.; Koezuka, M.; Sudoh, R. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 3095.
14. Sheldrick, G. M. *Acta Crystallogr*., *Sect. A: Found. Adv.* **2008**, *A64*, 112.