Synthesis of dispiro heteroanalogs of pyrrolizidine alkaloids: crystal and molecular structure of substituted 3',4'',5-trioxodispiro[(2'',5''-cyclohexadiene)-1''(4''H),7'-[7H]pyrrolizine-2'(3'H),2-[2H]pyrrole]-1'-carboxamide

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Abstract
3-Aroyl-1H-pyrrolo[2,1-c][1,4]benzoxazine-1,2,4-triones react with substituted 2-(3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)acetamides to produce substituted 3',4'',5-trioxodispiro[(2'',5''-cyclohexadiene)-1''(4''H),7'-[7H]pyrrolizine-2'(3'H),2-[2H]pyrrole] systems. The crystal and molecular structure of substituted 3',4'',5-trioxodispiro[(2'',5''-cyclohexadiene)-1''(4''H),7'-[7H]pyrrolizine-2'(3'H),2-[2H]pyrrole]-1'-carboxamide was confirmed by X-ray analysis.

Keywords: 1H-Pyrrolo[2,1-c][1,4]benzoxazine-1,2,4-trione, 2-(3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)acetamide, heterocyclization, analogs of pyrrolizidine alkaloids

Introduction
The annulation of a pyrrol-dione cycle with a benzoxazine fragment led to the formation of the polycarbonylic heterocyclic 1H-pyrrolo[2,1-c][1,4]benzoxazine-1,2,4-trione system. Nucleophilic transformations of 3-aryloxy-1H-pyrrolo[2,1-c][1,4]benzoxazine-1,2,4-triones by the action of OH- and NH-monoo- and NH,OH-, and NH,SH-binucleophiles are convenient methods for the synthesis of carbonyl derivatives of five- and six-membered nitrogen-containing heterocycles, ensembles of such heterocycles, and fused heterocyclic systems.
Recently, we have described the interactions of 3-aroyl-1\(H\)-pyrrolo[2,1-\(c\)][1,4]benzoxazine-1,2,4-triones \(A\) with 4',5'-dihydro-2',5',5'-trimethyl-4\(H\)-spiro[naphthalene-1,3'-pyrrol]-4-one \(B\) and ethyl (2\(Z\))-2-(3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)-acetate \(C\) giving rise to substituted dispiro[naphthalene-1(4\(H\)),1'-[1\(H\)]pyrrolizine-6'(5'H),2''-[2\(H\)]pyrrole]-4,5',5''(1''\(H\))-triones \(D\) and a bridged 7'-oxa-2',12'-diazatetracyclo[6.5.1.0\(1\),5.0\(8\),12\]tetradecane system \(E\), respectively (Scheme 1). During continuing studies on analogous transformations, we have now examined the reaction of pyrrolobenzoxazinetrones with a spiro heterocyclic enamine containing an additional functional amide group NH\(2\) – substituted 2-(3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)acetamides.\(^9\) The latter possess three nucleophilic centers, \(\beta\)-CH and NH groups in the enamine moiety and an amide NH\(2\) group. Initial electrophilic attack at one of these centers should determine the structure of the final product.

Scheme 1. Formation of substituted dispiro[naphthalene-1(4\(H\)),1'-[1\(H\)]pyrrolizine-6'(5'H),2''-[2\(H\)]pyrrole]-4,5',5''(1''\(H\))-triones \(D\) and a bridged 7'-oxa-2',12'-diazatetracyclo [6.5.1.0\(1\),5.0\(8\),12\] tetradecane system \(E\).

Results and Discussion

3-Aroyl-1\(H\)-pyrrolo[2,1-\(c\)][1,4]benzoxazine-1,2,4-triones \(1a-e\) interacted with substituted 2-(3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)acetamides \(2a-c\),\(^9\) proceeding at a 1:1 molar ratio of reactants under reflux for 2-5 min in anhydrous acetonitrile (until the disappearance of the bright violet color typical of the initial compounds \(1\)) and resulted in the formation of substituted dispiro pyrrolizidines \(3a-o\) (Scheme 2). The structure of compound \(3f\) was confirmed by X-ray analysis (Figure 1).
Compounds 3a-o are light yellow crystalline substances readily soluble in dimethylsulfoxide (DMSO) and N,N-dimethylformamide (DMF), poorly soluble in alcohols, ethers, chlorocarbons, aromatics and insoluble in saturated hydrocarbons and water. They showed a positive color test result (cherry color) for phenolic and enolic hydroxyl group upon treatment with an alcoholic solution of FeCl₃.

The molecular structures of compounds 3a-o were confirmed with the help of spectroscopic and analytical data. For example, the IR spectra of 3a-o contained two stretching bands of an NH₂ group in the range of 3428-3496 and 3303-3383 cm⁻¹, respectively, a stretching band indicating enol OH group as broadened band in the range of 3088-3247 cm⁻¹, two stretching bands of C²⁻=O and C³⁻=O lactam carbonyl groups in the range of 1692-1746 cm⁻¹, stretching bands of C⁴⁻=O and CONH₂ carbonyl groups in the range of 1647-1671 cm⁻¹ and a stretching band indicating ArC=O carbonyl group at 1620-1634 cm⁻¹.

Analysis of compounds 3a-o by ¹H NMR spectra (DMSO-d₆) showed that, besides the signals inherent to the protons of aromatic rings and the substituents attached thereto, the spectra exhibited two singlets at δ 1.16–1.91 ppm due to six protons of two methyl groups at the C₅⁻ atom of the pyrrolidine moiety, a two doublets at δ 1.98–2.72 ppm due to the methylene protons at C⁶⁻ atom of the pyrrolidine moiety, a broadened a singlet at δ 5.67–6.37 ppm due to two protons of group NH₂, a singlet at δ 9.89–10.34 ppm due to proton of the phenolic group OH, and a singlet at δ 11.81–12.51 ppm due to proton of the enolic group OH.

We hypothesized that the described reaction involves the initial addition of an activated β-CH group of 2 to the C⁵⁻ in molecule 1, followed by pyrrole ring closure via intramolecular
attack by the NH group on the lactone carbonyl carbon atom C⁴ in the oxazine ring and opening of the latter at C⁴–O⁵, as has been described previously for the reaction of the same pyrrolobenzoxazinetriones with heterocyclic enamines: 1-methyl-3,4-dihydroisoquinolines¹⁰,¹¹ 2′,5′,5′-trimethyl-4′,5′-dihydro-4H-spiro[naphthalene-1,3′-pyrrol]-4-one.⁶ It should be noted that the most favorable nucleophilic reaction center is the acetamide group NH₂ (Nδ -0.400 for compound 2a, Nδ -0.401 for compound 2b, Nδ -0.402 for compound 2c), according to semiempirical AM1 quantum-chemical calculations (Hyperchem 8.0 software package), but not the β-CH group (Cδ -0.040 for compound 2a, Cδ -0.061 for compound 2b, Cδ -0.040 for compound 2c) or NH group (Nδ -0.122 for compound 2a, Nδ -0.138 for compound 2b, Nδ -0.130 for compound 2c) of the enamine fragment. However, the NH₂ group does not participate in the course of this interaction.

**Figure 1.** The molecular structure of 3-benzoyl-5′,6′-dihydro-4-hydroxy-1-(2-hydroxyphenyl)-5″-methoxy-2″,5′,5′-trimethyl-3′,4″,5-trioxodispiro[2″,5″-cyclohexadiene]-1″(4″H),7″- [7H]pyrrozoline-2′(3′H),2-[2H]pyrrole]--1′-carboxamide 3f.

**Crystallographic data.** According to the X-ray data, compound 3f crystallizes in the centrosymmetric space group of a monoclinic system as a solvate with acetonitrile (1:1). The molecule has a complicated stereochemistry (Figure 1), so only heteroatoms are marked in Figure 1 for clarity. All bond distances and angles are typical for this class of compound. In the crystal packing, a system of intramolecular H-bonds with the participation of CONH₂, OH and C=O groups is present.
Conclusions

The described interaction may be regarded as an example of a regioselective synthetic pathway to a previously inaccessible dispiro heterocyclic system with various substituents in several positions of both heterocyclic fragments. The products may be regarded as dispiro heterocyclic analogs of pyrrolizidine alkaloids. Derivatives of pyrrolizidine alkaloids exhibit important pharmacological properties; among these, the most significant are indicine N-oxide, platiphillin, and sarracine, which are important antitumor and spasmyloytic drugs.

Experimental Section

General. The IR spectra were recorded in mineral oil on an IFS 66 (Bruker) spectrophotometer. The $^1$H NMR and $^{13}$C NMR spectra were recorded at 300 MHz on a Mercury-300BB instrument with dimethylsulfoxide (DMSO-$d_6$) [for compounds 3a–o] or CDCl$_3$ [for compounds 2a,b] as solvents and HMDS as the internal standard. The mass spectra were obtained on a Kratos MS-30 (UK) spectrometer (electron impact, 70 eV). Elemental analyses for C, H and N were obtained using a LECO CHNS-932 analyzer.

General procedure, exemplified by 2-(3,3,6,9-tetramethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)acetamide (2a). 5.0 mmol of cyanoacetic acid amide was dissolved in 4 ml of 92% H$_2$SO$_4$, then under ice-cold water, 5.0 mmol of 2,5-dimethylanisole and 7.5 mmol of isobutyril aldehyde in 1 ml of CH$_2$Cl$_2$ were added. The mixture was stirred for 20 min at room temperature, then poured into a mixture of ice and 25 ml of aqueous ammonia. The resulting solid precipitate after neutralization was filtered off and purified by recrystallization from an ethanol-acetone mixture. 2a. Light yellow crystals (from EtOH-(Me)$_2$CO), yield 61%, mp 197.5-198.5 °C; IR ($v_{max}$, cm$^{-1}$): 3412, 3286, 1659, 1629. $^1$H NMR (300.1 MHz, DMSO-$d_6$): $\delta_{H}$ 1.44 (3H, s, C$_3$CH$_3$), 1.46 (3H, s, C$_3$CH$_3$), 1.87 (3H, s, CH$_3$), 1.94 (3H, s, CH$_3$), 1.97 (1H, d, H$_{A}$), 2.15 (1H, d, H$_{B}$), 2.16 (2J$_{HH}$ 14.3 Hz), 4.03 (1H, s, =CH-), 5.04 (2H, bs, NH$_2$), 6.14 (1H, s, H$^{10}$), 6.68 (1H, s, H$^{7}$), 8.49 (1H, bs, NH). MS, m/z (%): 260 [M]$^+$ (63.9), 245 [M-Me]$^+$ (17.1), 228 (19.4), 216 [M-CO(NH$_2$)]$^+$ (8.4), 200 (13.9), 176 [M-NHCH=CHCO(NH$_2$)]$^+$ (100), 161 (100), 146 (9), 134 (24.8), 121 (36.1), 103 (5.8), 91 (21.9), 85 (24.8), 77 (10). Anal. Calcld for C$_{15}$H$_{20}$N$_2$O$_2$ (260.33): C, 69.20; H, 7.74; N, 10.76%. Found: C, 69.27; H, 7.35; N, 10.71%.

2-(9-methoxy-3,3,6-trimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)acetamide (2b). 2.0 mmol of cyanoacetic acid amide was dissolved in 2 ml of 92% H$_2$SO$_4$, then under ice-cold water, 5.0 mmol of 2,5-dimethylanisole and 7.5 mmol of isobutyril aldehyde were added. The mixture was stirred for 20 min at room temperature, then poured into a mixture of ice and 7 ml of aqueous ammonia, and extracted with methylene chloride (3 × 10 ml). The combined extracts
were dried over MgSO₄, the solvent was distilled off, and the residue was crystallized from isopropanol.

Light yellow crystals (from isopropanol), yield 44%, mp 208-210 °C; IR (νmax, cm⁻¹): 3398, 3327, 3012, 1650, 1566. ¹H NMR (300 MHz, CDCl₃): δH 1.46 (3H, s, C³(CH₃)), 1.48 (3H, s, C³(CH₃)), 1.96 (3H, s, C³(CH₃)), 2.02 (1H, d, H⁺A, JHH 13.8 Hz), 2.23 (1H, d, H⁺B, JHH 13.8 Hz), 3.66 (3H, s, H₂CO-C⁹), 4.06 (1H, s, CH₃), 4.97 (2H, br s, NH₂), 5.48 (1H, s, H₁⁰), 6.18 (1H, s, H₇), 8.52 (1H, br s, NH). ¹³C NMR (75 MHz, CDCl₃): δC 19.61 (CH₂-C⁹), 30.84 and 32.09 (2CH₃-C₃), 46.68 (C₄), 54.85 (H₂CO-C⁹), 56.63, 61.15 (C¹, C³), 78.15 (CH=), 119.78 and 127.98 (C⁷, C¹⁰), 148.89 and 159.36 (C⁶, C⁸), 161.99 (C⁴), 172.49 (C=O), 180.95 (C=O). MS, m/z (%): 276 [M⁺] (17), 259 [M⁺-Me] (3), 245 [M⁺-OMe] (2), 192 [M⁺-NHC(CH)CONH₂] (83), 177 [M⁺-NHC(CH)CONH₂-Me] (100). Anal. Calcld. for C₁₃H₂₂N₂O₇ (276.15): C, 65.20; H, 7.30; N, 10.14%. Found: C, 64.96; H, 7.27; N, 9.78%.

General procedure, exemplified by 3-benzoyl-5′,6′-dihydro-4-hydroxy-1-(2-hydroxyphenyl)-2′,5′,5'-tetr methyl-3',4',5-trioxodispiro[2′,3′-cy clohexadiene]-1''(4'H),7'-[7H]pyrrolizine-2'(3'H),2-[2'H]pyrrole-1-carboxamide (3a). A solution of compounds 1a (1 mmol) and 2a (1 mmol) in dry acetonitrile (20 ml) was heated under reflux for 2 min and then allowed to cool. The resulting solid precipitate was filtered off and purified by recrystallization from ethylacetate.

3a. Light yellow crystals (from EtOAc), yield 89%, mp 253-254 °C; IR (νmax, cm⁻¹): 3457, 3350 (NH₂), 3162 w (OH), 1740, 1717 (C=O, C=O), 1663 (C=O, CONH₂), 1627 (COPh). ¹H NMR (300.1 MHz, DMSO-d₆): δH 1.27 (3H, s, CH₃), 1.55 (3H, s, CH₃), 1.69, 1.75 (6H, s, 2CH₃), 2.27 (1H, d, H⁺A, JHH 14.4 Hz), 2.48 (1H, d, H⁺B, JHH 14.4 Hz), 5.85 (2H, bs, NH₂), 6.02 (1H, s, CH), 6.79 (1H, s, CH), 6.86-7.85 (9H arom, m, 9CH), 9.92 (1H, s, OH, phenol), 12.44 (1H, bs, OH enol). Anal. Calcld. for C₃₃H₂₉N₂O₇ (579.60): C, 68.38; H, 5.04; N, 7.25%. Found: C, 68.24; H, 5.17; N, 7.25%.

5′,6′-Dihydro-4-hydroxy-1-(2-hydroxyphenyl)-2′,5′,5′'-tetr methyl-3-(4-methylbenzoyl)-3′,4′,5-trioxodispiro[2′,5′'-cyclohexadiene]-1''(4'H),7'-[7H]pyrrolizine-2'(3'H),2-[2'H]pyrrole-1-carboxamide (3b). Light yellow crystals (from EtOAc), yield 92%, mp 259-260 °C; IR (νmax, cm⁻¹): 3496, 3377 (NH₂), 3153 w (OH), 1742, 1695 (C=O, C=O), 1671 (C=O, CONH₂), 1627 (C=O, CONH₂), 1617 (C=O, CONH₂). ¹H NMR (300.1 MHz, DMSO-d₆): δH 1.27 (3H, s, CH₃), 1.55 (3H, s, CH₃), 1.69, 1.75 (6H, s, 2CH₃), 2.27 (1H, d, H⁺A, JHH 14.4 Hz), 2.48 (1H, d, H⁺B, JHH 14.4 Hz), 2.54 (3H, s, C₆H₃CH₃-4), 5.83 (2H, bs, NH₂), 6.01 (1H, s, CH), 6.77 (1H, s, CH), 6.85-7.76 (8H arom, m, 8CH), 9.89 (1H, s, OH, phenol), 12.45 (1H, bs, OH enol). Anal. Calcld. for C₃₄H₃₁N₃O₇ (593.63): C, 68.79; H, 5.26; N, 7.08%. Found: C, 68.72 ; H, 5.34; N, 6.97%.

5′,6′-Dihydro-4-hydroxy-1-(2-hydroxyphenyl)-3-(4-methoxybenzoyl)-2′,5′,5′'-tetr methyl-3',4',5-trioxodispiro[2′,5′'-cyclohexadiene]-1''(4'H),7'-[7H]pyrrolizine-2'(3'H),2-[2'H]pyrrole-1-carboxamide (3c). Light yellow crystals (from EtOAc), yield 86%, mp 270-271 °C; IR (νmax, cm⁻¹): 3465, 3371 (NH₂), 3088 w (OH), 1746, 1713 (C=O, C=O), 1665 (C=O, CONH₂), 1620 (COOC₆H₄OCH₃-4). ¹H NMR (300.1 MHz, DMSO-d₆): δH 1.27 (3H, s, CH₃), 1.56 (3H, s, CH₃), 1.69, 1.76 (6H, s, 2CH₃), 2.27 (1H, d, H⁺A, JHH 14.4 Hz), 2.47
(1H, d, H\textsuperscript{3}B, \textsuperscript{2}J\textsubscript{HH} 13.8 Hz), 3.89 (3H, s, C\textsubscript{6}H\textsubscript{4}OCH\textsubscript{3}-4), 5.83 (2H, bs, NH\textsubscript{2}), 6.01 (1H, s, CH), 6.77 (1H, s, CH), 6.86-7.87 (8H\textsubscript{arom}, m, 8CH), 9.89 (1H, s, OH, phenol), 12.40 (1H, bs OH enol).

Anal. Calcd for C\textsubscript{3}H\textsubscript{11}N\textsubscript{3}O\textsubscript{8} (609.63): C, 66.99; H, 5.13; N, 6.89%. Found: C, 66.92; H, 5.15; N, 6.74%.

3-(4-Chlorobenzoyl)-5'6'-dihydro-4-hydroxy-1-(2-hydroxyphenyl)-2',5',5',5''-tetramethyl-3',4',5-trioxodispiro[(2',5''-cyclohexadiene)-1''(4'\textprime H),7''-[7H]pyrrolizine-2'(3'H),2-\textsuperscript{[2H]}pyrrole]-1'-carboxamide (3d). Light yellow crystals (from EtOAc), yield 88%, mp 281-282 °C; IR (\textit{vmax}, cm\textsuperscript{-1}): 3476, 3376 (NH\textsubscript{2}), 3247 w (OH), 1743, 1715 (C\textsuperscript{=O}, C\textsuperscript{=O}), 1658 (C\textsuperscript{=O}, CONH\textsubscript{2}), 1634 (CO\textsubscript{2}H\textsubscript{4}Cl-4). \textsuperscript{1}H NMR (300.1 MHz, DMSO-d\textsubscript{6}): \textit{d}\textsubscript{H} 1.27 (3H, s, CH\textsubscript{3}), 1.54 (3H, s, CH\textsubscript{3}), 1.68, 1.75 (6H, s, 2CH\textsubscript{3}), 2.27 (1H, d, H\textsuperscript{6}A, \textsuperscript{2}J\textsubscript{HH} 13.8 Hz), 2.47 (1H, d, H\textsuperscript{6}B, \textsuperscript{2}J\textsubscript{HH} 14.4 Hz), 5.87 (2H, bs, NH\textsubscript{2}), 6.01 (1H, s, CH), 6.78 (1H, s, CH), 6.85-7.88 (8H\textsubscript{arom}, m, 8CH), 9.91 (1H, s, OH, phenol), 12.49 (1H, bs OH enol). Anal. Calcd for C\textsubscript{3}H\textsubscript{28}ClN\textsubscript{3}O\textsubscript{7} (614.04): C, 64.55; H, 4.60; N, 6.84%. Found: C, 64.45; H, 4.68; N, 6.74%.

3-(4-Bromobenzoyl)-5'6'-dihydro-4-hydroxy-1-(2-hydroxyphenyl)-2',5',5',5''-tetramethyl-3',4',5-trioxodispiro[(2',5''-cyclohexadiene)-1''(4'\textprime H),7''-[7H]pyrrolizine-2'(3'H),2-\textsuperscript{[2H]}pyrrole]-1'-carboxamide (3e). Light yellow crystals (from EtOAc), yield 92%, mp 280-281 °C; IR (\textit{vmax}, cm\textsuperscript{-1}): 3428, 3302 (NH\textsubscript{2}), 3242 w (OH), 1743, 1713 (C\textsuperscript{=O}, C\textsuperscript{=O}), 1665 (C\textsuperscript{=O}, CONH\textsubscript{2}), 1633 (CO\textsubscript{2}H\textsubscript{4}Br-4). \textsuperscript{1}H NMR (300.1 MHz, DMSO-d\textsubscript{6}): \textit{d}\textsubscript{H} 1.28 (3H, s, CH\textsubscript{3}), 1.55 (3H, s, CH\textsubscript{3}), 1.68, 1.75 (6H, s, 2CH\textsubscript{3}), 2.27 (1H, d, H\textsuperscript{6}A, \textsuperscript{2}J\textsubscript{HH} 14.1 Hz), 2.47 (1H, d, H\textsuperscript{6}B, \textsuperscript{2}J\textsubscript{HH} 14.1 Hz), 5.83 (2H, bs, NH\textsubscript{2}), 6.01 (1H, s, CH), 6.78 (1H, s, CH), 6.85-7.80 (8H\textsubscript{arom}, m, 8CH), 9.91 (1H, s, OH, phenol), 12.51 (1H, bs OH enol). Anal. Calcd for C\textsubscript{3}H\textsubscript{28}BrN\textsubscript{3}O\textsubscript{7} (658.50): C, 60.19; H, 4.29; N, 6.38%. Found: C, 60.02; H, 4.35; N, 6.27%.

3-Benzoyl-5'6'-dihydro-4-hydroxy-1-(2-hydroxyphenyl)-5''-methoxy-2',5',5'-trimethyl-3',4',5-trioxodispiro[(2',5''-cyclohexadiene)-1''(4'\textprime H),7''-[7H]pyrrolizine-2'(3'H),2-\textsuperscript{[2H]}pyrrole]-1'-carboxamide (3f). Light yellow crystals (from EtOAc), yield 90%, mp 220-222 °C; IR (\textit{vmax}, cm\textsuperscript{-1}): 3465, 3361 (NH\textsubscript{2}), 3175 w (OH), 1744, 1713 (C\textsuperscript{=O}, C\textsuperscript{=O}), 1662 (C\textsuperscript{=O}, CONH\textsubscript{2}), 1625 (COPh). \textsuperscript{1}H NMR (300.1 MHz, DMSO-d\textsubscript{6}): \textit{d}\textsubscript{H} 1.38 (3H, s, CH\textsubscript{3}), 1.68, 1.91 (6H, s, 2CH\textsubscript{3}), 2.27 (1H, d, H\textsuperscript{6}A, \textsuperscript{2}J\textsubscript{HH} 13.8 Hz), 2.72 (1H, d, H\textsuperscript{6}B, \textsuperscript{2}J\textsubscript{HH} 14.1 Hz), 3.48 (3H, s, OCH\textsubscript{3}), 5.20 (1H, s, CH), 5.82 (2H, bs, NH\textsubscript{2}), 6.03 (1H, s, CH), 6.90-7.89 (9H\textsubscript{arom}, m, 9CH), 9.92 (1H, s, OH, phenol), 12.42 (1H, bs, OH enol). Anal. Calcd for C\textsubscript{3}H\textsubscript{29}N\textsubscript{3}O\textsubscript{8} (595.60): C, 66.55; H, 4.91; N, 7.06%. Found: C, 66.54; H, 5.02; N, 6.95%.

X-ray diffraction study of the compound (3f). X-ray analysis of 3f including data collection, cell refinement and data reduction was carried out with an Oxford Diffraction Xcalibur SCCD diffractometer using CrysalisPro software package\textsuperscript{13}. Analysis was accomplished on standard procedure (monochromatic MoK\textalpha-irradiation, \omega-scanning with steps 1°, 295(5) K). Absorption correction was not applied (\mu = 0.094 mm\textsuperscript{-1}). According to X-Ray data the crystal is monoclinic, the space group C2/c, a = 29.4226(8) Å, b = 16.8116(11) Å, c = 14.2177(13) Å, \beta = 113.527(19)°. \theta range for data collection: 2.86 to 26.38°. 6587 Reflections were collected, 2369 reflections with I>2\sigma(I), completeness 99.7%. The structure was solved by the direct method.
and refined by full-matrix least-squares on F² method using SHELXTL program package. Results of refinement: R₁ = 0.0531, wR₂ = 0.1239 (for >2σ(I)), R₁ = 0.1253, wR₂ = 0.1288 (for all data), S = 1.003, largest diff. peak and hole 0.248 and -0.457 eÅ⁻³.

5′6′-Dihydro-4-hydroxy-1-(2-hydroxyphenyl)-5″'-methoxy-2″',5″',5″'-trimethyl-3-(4-methylbenzoyl)-3′,4′,5-trioxodispiro[2″',5″'-cyclohexadiene]-1″'(4″',H)₇'-[7]H]pyrrolizine-2′(3'H),2-[2'H]pyrrole-1′-carboxamide (3g). Light yellow crystals (from EtOAc), yield 87%, mp 228-230 °C; IR (νmax, cm⁻¹): 3479, 3356 (NH₂), 3168 w (OH), 1740, 1701 (C=O, C=O), 1663 (C=O, CONH₂), 1626 (COCH₂CH₃-4). ¹H NMR (300.1 MHz, DMSO-d₆): δH 1.35 (3H, s, CH₃), 1.55, 1.73 (6H, s, 2CH₃), 2.27 (1H, d, H^6''ₐ, JₗHH 13.8 Hz), 2.71 (1H, d, H^6''ₗ, JₗHH 14.4 Hz), 2.42 (3H, s, CH₃CH₂-4), 3.48 (3H, s, OCH₃), 5.90 (2H, bs, NH₂), 5.95 (1H, s, CH), 6.03 (1H, s, CH), 6.85-7.80 (8Hₐrom, m, 8CH), 9.90 (1H, s, OH, phenol), 12.44 (1H, bs, OH enol). Anal. Calcd for C₃₄H₃₁N₃O₈ (609.63): C, 66.99; H, 5.13; N, 6.89%. Found: C, 66.91; H, 5.21; N, 6.88%.

5′6′-Dihydro-4-hydroxy-1-(2-hydroxyphenyl)-5″'-methoxy-3-(4-methoxybenzoyl)-2″',5″',5″'-trimethyl-3′,4′,5-trioxodispiro[2″',5″'-cyclohexadiene]-1″'(4″',H)₇'-[7]H]pyrrolizine-2′(3'H),2-[2'H]pyrrole-1′-carboxamide (3h). Light yellow crystals (from EtOAc), yield 82%, mp 216-218 °C; IR (νmax, cm⁻¹): 3482, 3354 (NH₂), 3157 w (OH), 1740, 1713 (C=O, C=O), 1665 (C=O, CONH₂), 1625 (COCH₂CH₂OCH₃-4). ¹H NMR (300.1 MHz, DMSO-d₆): δH 1.35 (3H, s, CH₃), 1.55, 1.73 (6H, s, 2CH₃), 2.31 (1H, d, H^6''ₐ, JₗHH 14.1 Hz), 2.54 (1H, d, H^6''ₗ, JₗHH 14.1 Hz), 3.48 (3H, s, OCH₃), 3.89 (3H, s, CH₃CH₂OCH₃-4), 5.94 (1H, s, CH), 5.97 (2H, bs, NH₂), 6.02 (1H, s, CH), 6.85-7.88 (8Hₐrom, m, 8CH), 9.90 (1H, s, OH, phenol), 12.47 (1H, bs, OH enol). Anal. Calcd for C₃₄H₃₁N₃O₈ (625.62): C, 65.27; H, 4.99; N, 6.72%. Found: C, 65.15; H, 5.19; N, 6.70%.

3-(4-Chlorobenzoyl)-5′6′-dihydro-4-hydroxy-1-(2-hydroxyphenyl)-5″'-methoxy-2″',5″',5″'-trimethyl-3′,4′,5-trioxodispiro[2″',5″'-cyclohexadiene]-1″'(4″',H)₇'-[7]H]pyrrolizine-2′(3'H),2-[2'H]pyrrole-1′-carboxamide (3i). Light yellow crystals (from EtOAc), yield 88%, mp 225-227 °C; IR (νmax, cm⁻¹): 3467, 3350 (NH₂), 3242 w (OH), 1740, 1718 (C=O, C=O), 1665 (C=O, CONH₂), 1630 (COCH₂Cl-4). ¹H NMR (300.1 MHz, DMSO-d₆): δH 1.37 (3H, s, CH₃), 1.67, 1.91 (6H, s, 2CH₃), 2.27 (1H, d, H^6''ₐ, JₗHH 13.8 Hz), 2.71 (1H, d, H^6''ₗ, JₗHH 14.4 Hz), 3.41 (3H, s, OCH₃), 5.20 (1H, s, CH), 5.85 (2H, bs, NH₂), 6.04 (1H, s, CH), 6.87-7.92 (8Hₐrom, m, 8CH), 9.92 (1H, s, OH, phenol), 12.50 (1H, bs OH enol). Anal. Calcd for C₃₃H₂₈ClN₃O₈ (630.04): C, 62.91; H, 4.48; N, 6.67%. Found: C, 62.80; H, 4.53; N, 6.53%.

3-(4-Bromobenzoyl)-5′6′-dihydro-4-hydroxy-1-(2-hydroxyphenyl)-5″'-methoxy-2″',5″',5″'-trimethyl-3′,4′,5-trioxodispiro[2″',5″'-cyclohexadiene]-1″'(4″',H)₇'-[7]H]pyrrolizine-2′(3'H),2-[2'H]pyrrole-1′-carboxamide (3j). Light yellow crystals (from EtOAc), yield 92%, mp 271-272 °C; IR (νmax, cm⁻¹): 3479, 3356 (NH₂), 3157 w (OH), 1743, 1704 (C=O, C=O), 1662 (C=O, CONH₂), 1627 (COCH₂Br-4). ¹H NMR (300.1 MHz, DMSO-d₆): δH 1.35 (3H, s, CH₃), 1.54, 1.71 (6H, s, 2CH₃), 2.32 (1H, d, H^6''ₐ, JₗHH 14.1 Hz), 2.54 (1H, d, H^6''ₗ, JₗHH 13.9 Hz), 3.48 (3H, s, OCH₃), 5.95 (1H, s, CH), 5.96 (2H, bs, NH₂), 6.03 (1H, s, CH), 6.85-7.81
(8H$_{\text{arom}}$, m, 8CH), 9.91 (1H, s, OH, phenol), 12.49 (1H, bs OH enol). Anal. Calcd for C$_{33}$H$_{28}$BrN$_3$O$_8$ (674.49): C, 58.76; H, 4.18; N, 6.23%. Found: C, 58.70; H, 4.18; N, 6.06%.

3-Benzoyl-5'6'-dihydro-4-hydroxy-1-(2-hydroxyphenyl)-5',5'-dimethyl-3',4''',5'-trioxodispiro[naphthalene-1''(4''H),7''-[7H]pyrrolizine-2'(3'H),2-[2H]pyrrole]-1'-carboxamide (3k). Light yellow crystals (from EtOAc), yield 79%, mp 214-216 °C; IR (v$_{\text{max}}$, cm$^{-1}$): 3463, 3354 (NH$_2$), 3162 w (OH), 1743, 1703 (C$^5$=O, C$^7$=O), 1662 (C$^{4'''}$=O, CONH$_2$), 1625 (COPh). $^1$H NMR (300.1 MHz, DMSO-d$_6$): δ$_H$ 1.18 (3H, s, CH$_3$), 1.47 (3H, s, CH$_3$), 1.98 (1H, d, H$^6''$, $^2$J$_{HH}$ 13.5 Hz), 2.16 (1H, d, H$^6''$, $^2$J$_{HH}$ 13.8 Hz), 6.37 (2H, bs, NH$_2$), 6.18 (1H, d, CH), 6.61 (1H, d, CH), 6.83-7.15 (13H$_{\text{arom}}$, m, 13CH), 10.32 (1H, s, OH, phenol), 11.87 (1H, bs, OH enol). Anal. Calcd for C$_{35}$H$_{27}$N$_3$O$_7$ (601.60): C, 69.88; H, 4.52; N, 6.98%. Found: C, 69.83; H, 4.61; N, 6.92%.

5'6'-Dihydro-4-hydroxy-1-(2-hydroxyphenyl)-5',5'-dimethyl-3-(4-methylbenzoyl)-3',4''',5'-trioxodispiro[naphthalene-1''(4''H),7''-[7H]pyrrolizine-2'(3'H),2-[2H]pyrrole]-1'-carboxamide (3l). Light yellow crystals (from EtOAc), yield 82%, mp 216-218 °C; IR (v$_{\text{max}}$, cm$^{-1}$): 3495, 3376 (NH$_2$), 3164 w (OH), 1746, 1700 (C$^5$=O, C$^7$=O), 1659 (C$^{4'''}$=O, CONH$_2$), 1627 (COC$_6$H$_4$CH$_3$-4). $^1$H NMR (300.1 MHz, DMSO-d$_6$): δ$_H$ 1.18 (3H, s, CH$_3$), 1.46 (3H, s, CH$_3$), 1.98 (1H, d, H$^6''$, $^2$J$_{HH}$ 13.5 Hz), 2.16 (1H, d, H$^6''$, $^2$J$_{HH}$ 13.8 Hz), 2.42 (3H, s, C$_6$H$_4$CH$_3$-4), 5.73 (2H, bs, NH$_2$), 6.18 (1H, d, CH), 6.59 (1H, d, CH), 6.84-8.06 (12H$_{\text{arom}}$, m, 12CH), 10.34 (1H, s, OH, phenol), 11.93 (1H, bs, OH enol). Anal. Calcd for C$_{36}$H$_{29}$N$_3$O$_7$ (615.63): C, 70.23; H, 4.75; N, 6.83%. Found: C, 70.22; H, 4.95; N, 6.65%.

5'6'-Dihydro-4-hydroxy-1-(2-hydroxyphenyl)-3-(4-methoxybenzoyl)-5',5'-dimethyl-3',4''',5'-trioxodispiro[naphthalene-1''(4''H),7''-[7H]pyrrolizine-2'(3'H),2-[2H]pyrrole]-1'-carboxamide (3m). Light yellow crystals (from EtOAc), yield 84%, mp 219-221 °C; IR (v$_{\text{max}}$, cm$^{-1}$): 3472, 3349 (NH$_2$), 3171 w (OH), 1743, 1692 (C$^5$=O, C$^7$=O), 1665 (C$^{4'''}$=O, CONH$_2$), 1625 (COC$_6$H$_4$OCH$_3$-4). $^1$H NMR (300.1 MHz, DMSO-d$_6$): δ$_H$ 1.16 (3H, s, CH$_3$), 1.46 (3H, s, CH$_3$), 1.98 (1H, d, H$^6''$, 2$^2$J$_{HH}$ 13.8 Hz), 2.16 (1H, d, H$^6''$, 2$^2$J$_{HH}$ 13.9 Hz), 3.91 (3H, s, C$_6$H$_4$OCH$_3$-4), 6.19 (1H, d, CH), 6.36 (2H, bs, NH$_2$), 6.57 (1H, d, CH), 6.81-8.05 (12H$_{\text{arom}}$, m, 12CH), 10.33 (1H, s, OH, phenol), 11.81 (1H, bs, OH enol). Anal. Calcd for C$_{36}$H$_{29}$N$_3$O$_8$ (631.63): C, 68.46; H, 4.63; N, 6.65%. Found: C, 68.31; H, 4.75; N, 6.46%.

3-(4-Chlorobenzoyl)-5'6'-dihydro-4-hydroxy-1-(2-hydroxyphenyl)-5',5'-dimethyl-3',4''',5'-trioxodispiro[naphthalene-1''(4''H),7''-[7H]pyrrolizine-2'(3'H),2-[2H]pyrrole]-1'-carboxamide (3n). Light yellow crystals (from EtOAc), yield 82%, mp 220-222 °C; IR (v$_{\text{max}}$, cm$^{-1}$): 3447, 3345 (NH$_2$), 3226 w (OH), 1724, 1702 (C$^5$=O, C$^7$=O), 1647 (C$^{4'''}$=O, CONH$_2$), 1626 (COC$_6$H$_4$Cl-4). $^1$H NMR (300.1 MHz, DMSO-d$_6$): δ$_H$ 1.59 (3H, s, CH$_3$), 1.68 (3H, s, CH$_3$), 2.47 (1H, d, H$^6''$, 2$^2$J$_{HH}$ 13.8 Hz), 2.68 (1H, d, H$^6''$, 2$^2$J$_{HH}$ 14.4 Hz), 5.68 (2H, bs, NH$_2$), 6.12 (1H, d, CH), 6.34 (1H, d, CH), 6.95-7.85 (12H$_{\text{arom}}$, m, 12CH), 9.89 (1H, s, OH, phenol), 11.95 (1H, bs OH enol). Anal. Calcd for C$_{35}$H$_{26}$ClN$_3$O$_7$ (636.05): C, 66.09; H, 4.12; N, 6.61%. Found: C, 65.95; H, 4.25; N, 6.61%.

3-(4-Bromobenzoyl)-5'6'-dihydro-4-hydroxy-1-(2-hydroxyphenyl)-5',5'-dimethyl-3',4''',5'-trioxodispiro[naphthalene-1''(4''H),7''-[7H]pyrrolizine-2'(3'H),2-[2H]pyrrole]-1'-
carboxamide (3o). Light yellow crystals (from EtOAc), yield 86%, mp 219-220 °C; IR (νmax, cm⁻¹): 3447, 3383 (NH₂), 1725, 1703 (C=O, C=O), 1647 (C=N=O, CONH₂), 1623 (COC₆H₄Br-4). ¹H NMR (300.1 MHz, DMSO-d₆): δH 1.59 (3H, s, CH₃), 1.68 (3H, s, CH₃), 2.47 (1H, d, H₆′A, JHH 14.4 Hz), 2.68 (1H, d, H₆′B, JHH 14.1 Hz), 5.67 (2H, bs, NH₂), 6.12 (1H, d, CH), 6.34 (1H, d, CH), 6.95-7.86 (12H arom, m, 12CH), 9.89 (1H, s, OH, phenol), 11.90 (1H, bs OH enol). Anal. Calcd for C₃₅H₂₆BrN₃O₇ (680.50): C, 61.77; H, 3.85; N, 6.17%. Found: C, 61.70; H, 3.93; N, 6.06%.

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