Synthesis and properties of α-bromonarceine imide and its derivatives

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By bromination of narceine imide in chloroform α-bromonarceine imide was prepared from which by the Hofmann degradation an imide of α-bromonarceonic acid was obtained. Also, a cyclization of synthesized vinyl derivatives of narceine imide and α-bromonarceine imide and an *N*-alkylation using benzyl chloride in potassium *tert*-butoxide have been studied.

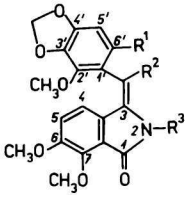
Был приготовлен α-бромнарцеинимид бромированием нарцеинимида в хлороформе. Из него был получен имид α-бромнарцеинной кислоты отщеплением по Гофману. Были изучены также циклизация синтезированных винил производных нарцеинимида и α-бромнарцеинимида и *N*-алкилирование с использованием бензилхлорида в *трет*-бутилате калия.

Z-Narceine imide (*1*) isolated from the mixture of opium alkaloids [1], as well as prepared synthetically [2] was used as a starting compound for the preparation of a series of new compounds [3—5] exhibiting interesting biological activities [6, 7]. In the present work we are concerned with the preparation of α-bromonarceine imide (*2*) and its derivatives.

Narceine imide easily adds halogens; in chloroform at 0°C it adds bromine to form an unstable dibromo derivative, from which eliminated hydrogen bromide being bound to the dimethylaminoethyl group of the molecule and α-bromonarceineimidium bromide separated from the solution; the base *2* was obtained by solving the bromide in hot water and by treatment with ammonium hydroxide. As in molecule *1* and *2* an asymmetrically substituted double bond is present, both compounds can exist in two isomeric *E* and *Z* forms. The prevailing *Z* form of *1* in solution is unstable and in the light is isomerized to *E* form of *3* [8]. This phenomenon was not observed with α-bromonarceine imide and the prepared compound *2* was a single product.

Ultraviolet spectra of geometric isomers (*1* and *3*) similarly as those of the isomers of 3-benzylidenephthalimidine [9] and 3-benzylidenephthalide [10] have

Compound	R^1	R^2	R^3
1	$CH_2CH_2N(CH_3)_2$	H	H
7	$CH=CH_2$	H	H
9	$CH_2CH_2N(CH_3)COCH_3$	H	H
11	CH_2CH_3	H	H
13	$CH_2CH_2N(CH_3)_2$	NO_2	H
15	$CH=CH_2$	H	$CH_2C_6H_5$



Compound	R^1	R^2	R^3
2	$CH_2CH_2N(CH_3)_2$	Br	H
3	$CH_2CH_2N(CH_3)_2$	H	H
4	$CH_2CH_2N^+(CH_3)_2O^-$	Br	H
5	$CH_2CH_2N^+(CH_3)_3I^-$	Br	H
6	$CH=CH_2$	Br	H
8	$CHBrCH_2Br$	Br	H
10	$CH_2CH_2N(CH_3)COCH_3$	Br	H
12	CH_2CH_3	Br	H
14	$CH=CH_2$	Br	$CH_2C_6H_5$
16	$CH=CH_2$	H	$CH_2C_6H_5$
17	$CH(CH_3)OCH_2CH_3$	H	$CH_2C_6H_5$

been observed to be different. The bands at the longest wavelengths were observed at 350 nm, log ε 4.24 for *1*, and at 345 nm, log ε 4.04 for *3* [4].

The longest wavelength band in the u.v. spectrum of *2* was observed at 340 nm indicating that both benzene rings are mutually in the *cis* position. This assumption could not be confirmed unambiguously on the basis of analogy of u.v. spectra with the published spectra of similar compounds because the isolation of the *E* isomer of compound *2* was unsuccessful.

The structure of *2* was assigned on the basis of the ^{1}H-n.m.r. spectral measurements, mainly from the chemical shifts of H-4 and H-5 protons.

With *Z* isomer of *2* the H-4 and H-5 protons are shielded by the benzene ring of the benzylidene part of the molecule and therefore the position of their signals is observed in the higher magnetic field (6.85 and 6.21 p.p.m.). With *E* isomer, in consequence of a deshielding of H-4 and H-5 protons by the bromine atom the signals should be observed in the lower magnetic field as confirmed with compounds *10* (*Z* isomer 7.18 and 6.45 p.p.m., *E* isomer 7.80 and 7.35 p.p.m.) and with α-bromo-3-benzylidenephthalimidine (*Z* isomer 6.62 and 6.43 p.p.m., *E* isomer 8.78 and 7.60 p.p.m. [9]), respectively. From the mentioned data it follows that the prepared compound *2* is *Z* isomer.

In the i.r. spectrum of *2* the ν(C=O) bands of 5-membered lactam ring are observed at 1710 cm^{-1}, *i.e.* at higher wavenumber than that with narceine imide (*1*) (ν(C=O) 1690 cm^{-1}); the ν(N−H) bands at 3437 and 3247 cm^{-1}; the ν(C=C) at 1658 cm^{-1} — the double bond conjugated with the aromatic rings; the bands of the aromatic ring (1618 and 1510 cm^{-1}) and the ν(C−O−C) bands (1280, 1125, and 1095 cm^{-1}).

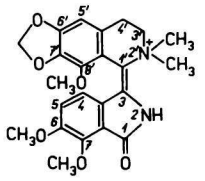
The mass spectrum of *2* is characterized by the presence of isotope peaks of the molecular ion radical at *m/z* 506 and 504 and a peak at *m/z* 425 ($M^{+\bullet}-$Br). The base peak at *m/z* 380 ($C_{21}H_{18}NO_6$, 380, 1134) was formed from the fragment by the loss of the dimethylamino group (425→380 *m** 339.8). The dimethylaminoethyl group in the side chain is indicated by the presence of a peak at *m/z* 58, $CH_2{=}N^+(CH_3)_2$.

Narceine imide *N*-oxide, formed by oxidation of narceine imide (*1*), afforded by the reaction with acetic anhydride two compounds: 7,8-dihydro-5*H*-isoindolo[1,2-*b*][3]benzazepin-5-one derivative [3] and *N*-methyl-*N*-acetyl derivative *9* [4]. Analogously, α-bromonarceine imide *N*-oxide *4* prepared by oxidation of α-bromonarceine imide *2* did not afford compound *10* but a desamination product was formed (*6*), identical with the compound obtained by the Hofmann degradation of methiodide *5*. The expected compound *10* was prepared by the bromination of *9*.

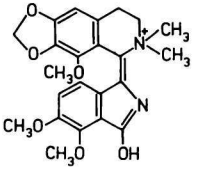
Vinyl halogenides of the α-bromobenzylidenephthalimidine type are less reactive [11], a substitution of halogen is possible only under relatively hard conditions.

In our work we were successful in synthesis of compound *13* in a low yield by the reaction with silver nitrate. The configuration of compound prepared was determined on the basis of ^{1}H-n.m.r. spectroscopy.

In solution by the action of light α-bromonarceine imide (*2*) afforded compound *21*. In the u.v. spectrum of compound *21* the longest wavelength band as compared with the starting compound *2* (340 nm) was bathochromically shifted (384 nm), which can be explained by the prolonged conjugation in consequence of the hindered rotation of the benzene ring of the benzylidene part of α-bromonarceine imide *2* by a closure of 6-membered isoquinoline ring.



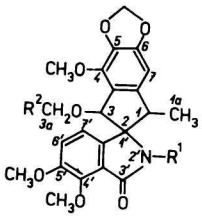
21a



21b

Compound *21* can exist in two tautomeric forms; we assume that in acidic medium a keto form *21a* prevails (375 nm, log ε 4.15), while in alkaline medium an enol form *21b* (397 nm, log ε 4.15) (an isosbestic point at 384 nm). This assumption was also confirmed by the i.r. spectrum of *21* in which the carbonyl band of the amide group at 1710 cm^{-1} is weak as compared with that of the starting compound *2*. On the other hand, the intensity of the band at 1640 cm^{-1} belonging to the environment of multiple bonds conjugated with the carbonyl group was increased. ^{1}H-N.m.r. and mass spectra confirm the suggested structure of *21*. Other derivatives of α-bromonarceine imide were prepared from *Z* imide of narceonic acid *7*. On hydrogenation of the terminal double bond of compound *7* by hydrazine compound *11* was obtained, which on bromination in chloroform afforded *Z* isomer *12*. By addition of bromine to the two double bonds of compound *7* tribromo derivative *8* has been prepared.

A further reactive centrum of molecule *2* is a lactam NH group, which on changing to the potassium salt by treatment with potassium *tert*-butoxide was alkylated by benzyl chloride; under the given reaction conditions a dimethylaminoethyl group was also quarternized by benzyl chloride and by the action of potassium *tert*-butoxide dimethylbenzylamine cleaved to form vinyl derivative *14*. Narceine imide (*1*) afforded vinyl derivative *15* in a similar manner. The compounds of the mentioned vinyl type easily cyclized in acidic medium [12, 13]. By refluxing the compound *7* in methanolic hydrochloric acid 55% of 6,7-dihydro-3,4,11-trimethoxy-7-methyl-9,10-methylenedioxy-5*H*-isoindolo[1,2-*b*]isoquinolo-5-one and 2% of methoxyspiro compound *18* [5] were obtained. In our work, by cyclization of *7* in ethanolic hydrochloric acid the opposite ratio of compounds obtained (64.8% of ethoxyspiro compound *19* and only 6% of 5*H*-isoindolo[1,2-*b*]isoquinolo-5-one derivative) was found. The proposed structure of *19* was also confirmed by ^{13}C-n.m.r. spectroscopy (Table 1).



Compound	R^1	R^2
18	H	H
19	H	CH_3
20	$CH_2C_6H_5$	CH_3

Table 1

Assignment of signals of ^{13}C-n.m.r. spectra of the alicyclic part of the molecule *19*

Carbon No.	δ/p.p.m.	Multiplicity
1	43.4	d
1a	10.8	q
2	72.9	s
3	81.7	d
3a	65.5	t
3b	15.5	q
3′	168.3	s

An attempt to cyclize *14* even after 4 h of refluxing failed; under the equal conditions vinyl derivative *15* first isomerized to *E* form of *16* and then added ethanol to form ethoxyderivative *17*. The assumed product of cyclization of vinyl derivative *15*, *N*-benzylspiro compound *20* was obtained by benzylation of *19* in potassium *tert*-butoxide.

Experimental

Melting points were determined on a Kofler hot stage, mass spectra were recorded with a JMS-100 D Jeol at an ionization energy 70 eV, u.v. spectra with a Specord UV VIS (Zeiss, Jena), i.r. spectra with a Specord IR 71 (Zeiss, Jena) in KBr tablets, ^{13}C-n.m.r. spectra with a FX-60 Jeol and ^{1}H-n.m.r. spectra with a BS 467 Tesla (using tetramethylsilane as an internal reference) instruments. For thin-layer chromatography Silufol UV-254 plates (Kavalier, Votice) and solvent systems S_1 (benzene—methanol 19 : 1), S_2 (chloroform), and S_3 (chloroform—methanol 9 : 1) were used.

(Z)-3-(α-Bromo-6'-dimethylaminoethyl-2'-methoxy-3',4'--methylenedioxybenzylidene)-6,7-dimethoxyisoindolin-1-one, α-bromonarceine imide (2)

To the solution of *1* (44 g; 0.103 mol) in chloroform (200 cm^3) a solution of bromine (18.1 g; 0.113 mol) in chloroform (50 cm^3) was added at 0°C during 15 min and the reaction mixture was stirred for further 30 min to exclude white precipitate. A suspension was diluted with chloroform, filtered off, and dried. Yield 36.40 g (60.3%) of hydrogen bromide *2* which was dissolved in water and the base was liberated by adjusting the pH to 9 by addition of concentrated NH_4OH. The excluded solid was filtered off, washed with water and crystallized from the mixture ethanol—water 2:1. Yield 29.81 g (57.4%) of compound *2*, R_f 0.08 (S_1), 0.12 (S_2), m.p. 179.5—180°C (ethanol), 213°C (hydrogen bromide), 149.5—150°C (picrate).

For $C_{23}H_{25}BrN_2O_6$ (505.4) calculated: 54.66% C, 4.99% H, 5.54% N; found: 54.58% C, 4.81% H, 5.53% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 220 (4.69), 264 (4.25), 340 (4.24), λ_{min}^{MeOH}/nm (log ε): 248 (4.24), 305 (3.85). IR spectrum, cm^{-1}: 3437, 3247, 1710, 1658, 1628, 1510, 1280, 1125, 1096. ^{1}H-NMR spectrum ($CDCl_3$), δ/p.p.m.: 8.05 (s, 1H) NH; 6.85 (d, 1H), 6.21 (d, 1H), ABq, H_4H_5, $J_{4,5}$ 8 Hz; 6.59 (s, 1H) $H_{5'}$; 5.96 (s, 2H) OCH_2O; 4.02 (s, 3H), 3.87 (s, 3H), 3.77 (s, 3H), 3 × OCH_3; 2.73—2.28 (m, 4H) CH_2CH_2; 2.10 (s, 6H) $N(CH_3)_2$. Mass spectrum, *m/z* (relative intensity, %): 506 (3.3), 504 (3.4), 425 (43), 380 (100), 379 (20), 366 (5), 352 (4), 235 (13), 192 (7), 58 (100).

(Z)-3-(α-Bromo-6'-dimethylaminoethyl-2'-methoxy-3',4'--methylenedioxybenzylidene)-6,7-dimethoxyisoindolin-1-one N-oxide (4)

Compound *2* (10 g; 0.02 mol) was dissolved in acetone (100 cm^3) and hydrogen peroxide (8 cm^3, 10% solution) was added, the mixture was refluxed for 1 h and allowed to stand at room temperature for 24 h, the solution was concentrated to 10 cm^3, diluted with water and by addition of sodium chloride a solid compound was obtained which was filtered off and crystallized from the mixture acetone—water 9:1. Yield 5.2 g (50.5%) of compound *4*, m.p. 116—118°C.

For $C_{23}H_{25}BrN_2O_7$ (521.4) calculated: 52.99% C, 4.82% H, 5.37% N; found: 52.78% C, 4.96% H, 5.27% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 221 (4.30), 268 (3.76), 342 (3.23); λ_{min}^{MeOH}/nm (log ε): 250 (3.00), 316 (3.06). IR spectrum, cm^{-1}: 3400, 3200, 1705, 1663, 1613, 1500, 1270, 1120, 1085, 1050.

(Z)-3-(α-Bromo-6'-ethenyl-2'-methoxy-3',4'-methylenedioxybenzylidene)--6,7-dimethoxyisoindolin-1-one (6)

Compound *2* (10.0 g; 0.02 mol) was dissolved in chloroform (100 cm^3) and methyl iodide (9.5 g; 0.067 mol) was added during 10 min, the mixture was shaken up, the excluded precipitate was filtered off, washed with chloroform and dried. Yield 12.3 g (96.0%) of methiodide *4*, m.p. 222°C, which was refluxed in 33% aqueous potassium hydroxide

(20 cm³) for 3 h. A solid was filtered off, washed with water, dried, and crystallized from benzene. Yield 2.7 g (31.3%) of compound *6*, R_f 0.13 (S_1), 0.20 (S_2), 0.68 (S_3), m.p. 192.0—193°C.

For $C_{21}H_{18}BrNO_6$ (460.3) calculated: 54.80% C, 3.94% H, 3.04% N; found: 54.68% C, 3.82% H, 2.97% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 276 (4.36), 343 (4.20), λ_{min}^{MeOH}/nm (log ε): 260 (4.30), 310 (3.90). IR spectrum, cm⁻¹: 3440, 3225, 1725, 1665, 1615, 1505, 1280, 1120, 1090, 1055. ^{1}H-NMR spectrum ($CDCl_3$), δ/p.p.m.: 8.00 (s, 1H) NH; 6.86 (d, 1H), 6.18 (d, 1H), ABq, H_4H_5, $J_{4,5}$ 8 Hz, 6.85 (s, 1H) $H_{5'}$; 5.98 (s, 2H) OCH_2O; 6.71 (dd, H_x), 5.52 (dd, H_a), 5.09 (dd, H_b), $CH_x{=}CH_aH_b$, J_{bx} 11 Hz, J_{bc} 1 Hz, J_{ax} 18 Hz, 3.99 (s, 3H), 3.88 (s, 3H), 3.77 (s, 3H) 3 × OCH_3. Mass spectrum, *m/z* (relative intensity, %): 461 (1), 459 (1), 381 (10), 380 (100), 365 (1), 190 (16).

(Z)-3-[α-Bromo-6'-(1",2"-dibromoethyl)-2'-methoxy-3',4'--methylenedioxybenzylidene]-6,7-dimethoxyisoindolin-1-one (8)

Compound *7* (25.9 g; 0.056 mol) prepared from narceine imide methiodide *2* was dissolved in chloroform (200 cm³) and at 0°C a solution of bromine (21.0 g; 0.13 mol) in chloroform (150 cm³) was added. The solution was stirred for 1 h, concentrated and washed with water to neutral reaction and by adding ethanol compound *8* was excluded, which was crystallized from benzene. Yield 30.1 g (86.2%), m.p. 184—186°C.

For $C_{21}H_{18}Br_3NO_6$ (620.1) calculated: 40.67% C, 2.92% H, 2.26% N; found: 41.28% C, 3.21% H, 2.50% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 276 (4.13), 346 (4.04), λ_{min}^{MeOH}/nm (log ε): 252 (4.10), 310 (3.48). IR spectrum, cm⁻¹: 3220, 1715, 1660, 1623, 1275, 1130, 1090, 1060. ^{1}H-NMR spectrum (DMSO-d_6), δ/p.p.m.: 6.86 (d, 1H), 6.23 (d, 1H), ABq, H_4H_5, $J_{4,5}$ 8 Hz, 7.00 (s, 1H) $H_{5'}$; 6.07 (s, 2H) OCH_2O; 5.47—5.13 (m, 1H) $C\underline{H}BrCH_2Br$; 3.40—3.20 (m, 2H) $CHBrC\underline{H}_2Br$; 3.89 (s, 3H), 3.72 (s, 3H), 3.70 (s, 3H) 3 × OCH_3. Mass spectrum, *m/z* (relative intensity, %): 623 (0.4), 621 (0.9), 619 (0.9), 617 (0.4), 541 (0.2), 539 (0.6), 537 (0.3), 535 (0.2), 461 (0.4), 459 (0.6), 457 (0.1), 380 (100).

3-(α-Bromo-6'-N-acetyl-N-methylaminoethyl-2'-methoxy-3',4'--methylenedioxy)benzylidene-6,7-dimethoxyisoindolin-1-one (10)

To compound *9* (2.18 g; 4.8 mmol) prepared from narceine imide *N*-oxide *4*, dissolved in chloroform (50 cm³) bromine (0.88 g; 5.5 mmol) was added. The solution was concentrated and the residue crystallized from ethanol. Yield 1.83 g (71.5%) of compound *10* as a mixture containing 65% of *Z* isomer and 35% of *E* isomer, m.p. 199—201°C.

For $C_{24}H_{25}BrN_2O_7$ (533.4) calculated: 54.04% C, 4.72% H, 5.25% N; found: 53.91% C, 4.63% H, 5.24% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 221 (4.73), 264 (4.27), 347 (4.26), λ_{min}^{MeOH}/nm (log ε): 251 (4.11), 313 (3.78). IR spectrum, cm⁻¹: 3420, 3200, 1710, 1650, 1625, 1500, 1275, 1210, 1090, 1050. ^{1}H-NMR spectrum (DMSO-d_6), δ/p.p.m.: 7.80 (d, 1H), 7.35 (d, 1H) ABq, $J_{4,5}$ 8 Hz, H_4H_5 of *E* isomer; 7.18 (d, 1H), 6.54 (d, 1H), ABq, $J_{4,5}$ 8 Hz, H_4H_5 of *Z* isomer. Mass spectrum, *m/z* (relative intensity, %): 534 (1), 532 (1), 453 (20), 380 (100), 366 (38), 352 (22), 338 (31), 192 (78), 190 (30), 178 (11), 86 (26), 44 (27).

(Z)-3-(α-Bromo-6'-ethyl-2'-methoxy-3',4'-methylenedioxy)benzylidene--6,7-dimethoxyisoindolin-1-one (12)

To a solution of compound *11* (0.32 g; 0.84 mmol), prepared by reduction of compound *7* with hydrazine [4], in chloroform (10 cm^3), bromine (0.12 g; 0.8 mmol) was added, after 1 h the solution was concentrated and the residue crystallized from benzene. Yield 0.305 g (79.0%) of compound *12*, m.p. 204°C.

For $C_{21}H_{20}BrNO_6$ (462.3) calculated: 54.56% C, 4.36% H, 3.03% N; found: 54.51% C, 4.28% H, 3.00% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 214 (4.54), 269 (4.12), 343 (4.12), λ_{min}^{MeOH}/nm (log ε): 251 (4.08), 310 (3.72). IR spectrum, cm^{-1}: 3415, 3205, 1710, 1660, 1615, 1495, 1270, 1220, 1050. ^{1}H-NMR spectrum ($CDCl_3$), δ/p.p.m.: 7.83 (s, 1H) NH; 6.78 (d, 1H), 6.13 (d, 1H), ABq, $H_4H_{5'}$, $J_{4,5}$ 8 Hz; 6.45 (s, 1H) $H_{5'}$; 5.97 (s, 2H) OCH_2O; 3.98 (s, 3H), 3.85 (s, 3H), 3.75 (s, 3H) $3\times OCH_3$, 2.50 (q, 2H) $C\underline{H}_2CH_3$, J 6 Hz; 0.95 (t, 3H) $CH_2C\underline{H}_3$, J 6 Hz.

3-(α-Nitro-6'-dimethylaminoethyl-2'-methoxy-3',4'--methylenedioxy)benzylidene-6,7-dimethoxyisoindolin-1-one (13)

Compound *2* (3.5 g; 6.9 mmol) was dissolved in 40 cm^3 of the mixture ethanol—water (3:1) and silver nitrate (2.0 g; 12 mmol) was added, the reaction mixture was heated for 1 h, the suspension was filtered off, the filtrate concentrated *in vacuo* and the remaining residue dissolved in benzene, filtrated and after concentration chromatographed on aluminium oxide (activity grade IV), using gradient elution of the mixture benzene—ethanol from 100:0 to 90:10. The zones were detected visually, the eluent containing compound *13* was concentrated and the residue crystallized from benzene. Yield 0.8 g (24.6%) of compound *13*, m.p. 70—72°C.

For $C_{23}H_{25}N_3O_8$ (471.48) calculated: 58.60% C, 5.34% H, 8.91% N; found: 58.41% C, 5.48% H, 8.78% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 294 (3.73), 344 (3.52). IR spectrum, cm^{-1}: 3405, 3220, 1720, 1613, 1495, 1270, 1085, 1055. ^{1}H-NMR spectrum ($CDCl_3$), δ/p.p.m.: 8.28 (s, 1H) NH; 7.26 (d, 1H), 7.03 (d, 1H), ABq, H_4H_5, $J_{4,5}$ 8 Hz; 6.30 (s, 1H) $H_{5'}$; 5.92 (s, 2H) OCH_2O; 3.97 (s, 3H), 3.80 (s, 3H), 3.60 (s, 3H) $3\times OCH_3$; 2.35—2.13 (m, 4H) CH_2CH_2N; 2.10 (s, 6H) $N(CH_3)_2$.

(Z)-2-Benzyl-3-(α-bromo-6'-ethenyl-2'-methoxy-3',4'--methylenedioxy)benzylidene-6,7-dimethoxyisoindolin-1-one (14)

Compound *2* (3.82 g; 8 mmol) was dissolved in a mixture containing 0.40 g (0.01 mol) of potassium in *tert*-butanol (120 cm^3) and to the mixture benzyl chloride (2.0 g; 0.017 mol) was added. The solution was refluxed for 1 h to separate potassium chloride. The suspension was diluted with water, extracted with diethyl ether (4×50 cm^3), the extract was dried, concentrated and the residue crystallized from methanol. Yield 1.62 g (39.0%) of compound *14*, m.p. 189—193°C.

For $C_{28}H_{24}BrNO_6$ (550.4) calculated: 61.10% C, 4.39% H, 2.54% N; found: 61.02% C, 4.28% H, 2.47% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 269 (4.37), 342 (4.09), λ_{min}^{MeOH}/nm

(log ε): 251 (4.27), 304 (3.87). ^{1}H-NMR spectrum ($CDCl_3$), δ/p.p.m.: 7.22—7.10 (m, 5H); H_{arom}; 7.11 (d, 1H), 6.47 (d, 1H), ABq, H_4H_5, $J_{4,5}$ 8 Hz; 6.56 (s, 1H) $H_{5'}$; 5.89 (s, 2H) OCH_2O; 6.37 (dd, H_a), 5.36 (dd, H_b), 4.96 (dd, H_c) $CH_a{=}CH_bH_c$, J_{ab} 11 Hz, J_{bc} 2 Hz, J_{ac} 18 Hz; 5.07 (s, 2H) $NCH_2C_6H_5$; 4.00 (s, 3H), 3.72 (s, 3H), 3.68 (s, 3H) 3 × OCH_3.

(Z)-2-Benzyl-3-(6'-ethenyl-2'-methoxy-3',4'-methylenedioxybenzylidene)--6,7-dimethoxyisoindolin-1-one (15)

To 0.6 g (0.015 mol) of potassium in *tert*-butanol (150 cm³) compound *1* (5.05 g; 0.01 mol) was added with stirring and after solving *1* benzyl chloride (2.97 g; 0.024 mol) was added. After 1 h of refluxing the reaction mixture was diluted with water, extracted with diethyl ether (4 × 50 cm³), the extract was concentrated and the residue crystallized from methanol. Yield 4.1 g (73.5%) of compound *15*, m.p. 150—151°C.

For $C_{28}H_{25}NO_6$ (471.5) calculated: 71.33% C, 5.34% H, 2.97% N; found: 71.02% C, 5.28% H, 2.95% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 276 (4.38), 350 (4.22), λ_{min}^{MeOH}/nm (log ε): 252 (4.19), 313 (3.98). IR spectrum, cm^{-1}: 1700, 1655, 1600, 1500, 1270, 1090, 1055. ^{1}H-NMR spectrum ($CDCl_3$), δ/p.p.m.: 7.33 (d, 1H), 7.03 (d, 1H), ABq, H_4H_5, $J_{4,5}$ 8 Hz; 7.16—6.75 (m, 5H) H_{arom}; 6.67 (s, 1H) Ar−CH=; 6.10 (s, 1H) $H_{5'}$; 5.97 (s, 2H) OCH_2O; 6.42 (dd, H_a, 5.40 (dd, H_b), 4.92 (dd, H_c) $CH_a{=}CH_bH_c$, J_{ab} 11 Hz, J_{ac} 17 Hz, J_{bc} 2 Hz; 4.67 (s, 2H) N-$CH_2C_6H_5$; 4.00 (s, 3H), 3.92 (s, 3H), 3.81 (s, 3H) 3 × OCH_3. Mass spectrum, *m/z* (relative intensity, %): 471 (100), 441 (15), 440 (51), 381 (27), 380 (96), 366 (33), 365 (17), 350 (15), 190 (17), 178 (15), 176 (11), 92 (72), 91 (86), 77 (65), 39 (82).

(E)-2-Benzyl-3-(6'-ethenyl-2'-methoxy-3',4'-methylenedioxybenzylidene)--6,7-dimethoxyisoindolin-1-one (16)

Compound *15* (1.5 g; 0.032 mol) in 2% ethanolic hydrochloric acid (250 cm³) was refluxed for 1 h, the solution was concentrated and the residue filtered off and recrystallized from ethanol. Yield 1.4 g (93.4%) of compound *16*, m.p. 206°C.

For $C_{28}H_{25}NO_6$ (471.5) calculated: 71.33% C, 5.34% H, 2.97% N; found: 69.34% C, 5.11% H, 3.06% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 269 (4.34), 343 (4.15), λ_{min}^{MeOH}/nm, (log ε): 253 (4.24), 303 (3.91). IR spectrum, cm^{-1}: 1700, 1650, 1600, 1505, 1272, 1090, 1055. ^{1}H-NMR spectrum ($CDCl_3$), δ/p.p.m.: 7.22 (s, 5H) H_{arom}; 7.13 (d, 1H), 6.52 (d, 1H) H_4H_5, $J_{4,5}$ 8 Hz; 6.72 (s, 1H) ArCH=; 6.42 (s, 1H) $H_{5'}$; 6.33 (dd, 1H, H_a), 5.30 (dd, 1H, H_b), 4.78 (dd, 1H, H_c) $CH_a{=}CH_bH_c$, J_{ab} 11 Hz, J_{bc} 2 Hz, J_{ac} 17 Hz; 5.02 (s, 2H) $NCH_2C_6H_5$; 4.00 (s, 3H), 3.73 (s, 3H), 3.60 (s, 3H) 3 × OCH_3. Mass spectrum was identical with the spectrum of compound *15*.

(E)-2-Benzyl-3-[6'-(1"-ethoxyethyl)-2'-methoxy-3',4'--methylenedioxybenzylidene]-6,7-dimethoxyisoindolin-1-one (17)

Compound *16* (1 g; 2.1 mmol) was refluxed in 2% ethanolic hydrochloric acid (150 cm^3). The solution was concentrated *in vacuo* and the residue crystallized from benzene. Yield 0.8 g (73.1%) of compound *17*, m.p. 70°C.

For $C_{30}H_{31}NO_7$ (517.5) calculated: 69.62% C, 6.04% H, 2.71% N; found: 69.30% C, 5.73% H, 2.64% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 269 (4.24), 346 (4.13), λ_{min}^{MeOH}/nm (log ε): 256 (4.22), 305 (3.91). IR spectrum, cm^{-1}: 1700, 1655, 1615, 1495, 1270, 1080, 1045. ^{1}H-NMR spectrum ($CDCl_3$), δ/p.p.m.: 7.22 (s, 5H) H_{arom}; 7.10 (d, 1H), 6.40 (d, 1H), ABq, H_4H_5, $J_{4,5}$ 8 Hz; 6.85 (s, 1H) ArC<u>H</u>=; 6.72 (s, 1H) $H_{5'}$; 5.89 (s, 2H) OCH_2O; 5.36 (q, 1H) C<u>H</u>(OCH_2CH_2)CH_3, *J* 6 Hz; 4.20 (s, 2H) N<u>CH_2</u>C_6H_5; 3.96 (s, 3H), 3.72 (s, 3H), 3.68 (s, 3H) 3 × OCH_3; 3.46 (q, 2H) O<u>CH_2</u>CH_3; 0.83 (d, 3H) CH(OCH_2CH_3)C<u>H_3</u>, *J* 6 Hz; 0.76 (t, 3H) OCH_2C<u>H_3</u>, *J* 7 Hz. Mass spectrum, *m/z* (relative intensity, %): 517 (38), 489 (14), 488 (48), 473 (38), 471 (48), 440 (3), 426 (52), 382 (97), 381 (34), 380 (100), 366 (66), 352 (10), 336 (12), 223 (46), 205 (46), 91 (72), 77 (64).

3-Ethoxy-4,4',5'-trimethoxy-1-methylspiro[1,3-dioxolo[4,5-f]indane--2,1'-isoindolin-3'-one] (19)

Compound *7* (2.5 g; 6.5 mmol) was refluxed in 2% ethanolic hydrochloric acid (500 cm^3), the solution was concentrated to 70 cm^3, filtered and the filtrate was concentrated to 30 cm^3 and allowed to crystallize. The excluded compound was recrystallized from ethanol. Yield 1.8 g (64.8%) of compound *19*, m.p. 236—238°C.

For $C_{23}H_{25}NO_7$ (427.4) calculated: 64.62% C, 5.90% H, 3.28% N; found: 64.30% C, 5.73% H, 3.24% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 213 (4.81), 296 (3.89), 309 sh (3.85), λ_{min}^{MeOH}/nm (log ε): 272 (3.52). IR spectrum, cm^{-1}: 3425, 3215, 1695, 1625, 1500, 1275, 1090, 1045. ^{1}H-NMR spectrum ($CDCl_3$), δ/p.p.m.: 6.73 (d, 1H), 5.96 (d, 1H), ABq, $H_{6'}H_{7'}$, $J_{6',7'}$ 8 Hz; 6.46 (s, 1H) NH; 6.36 (s, 1H) H_7; 5.87 (s, 2H) OCH_2O; 4.53 (q, 1H) H_1, *J* 5 Hz; 4.36 (s, 1H) H_3; 4.00 (s, 3H), 3.93 (s, 3H), 3.72 (s, 3H), 3 × OCH_3; 3.55 (q, 2H) O<u>CH_2</u>CH_3, *J* 6 Hz; 1.42 (3H, t) OCH_2C<u>H_3</u>, *J* 6 Hz; 0.89 (d, 3H) C-1,C<u>H_3</u>, *J* 5 Hz. Mass spectrum, *m/z* (relative intensity, %): 427 (31), 412 (26), 399 (18), 382 (38), 381 (100), 366 (40), 352 (11), 350 (11), 336 (10), 207 (10), 192 (38).

2'-Benzyl-3-ethoxy-4,4',5'-trimethoxy-1-methylspiro[1,3--dioxolo[4,5-f]indane-2,1'-isoindolin-3'-one] (20)

To a mixture of potassium (0.15 g; 3.9 mmol) and compound *19* (0.6 g; 1.4 mmol) in *tert*-butanol (50 cm^3) benzyl chloride (0.36 g; 2.9 mmol) was added and the solution was refluxed for 1 h. The reaction mixture was diluted with water (100 cm^3), extracted with diethyl ether (4 × 30 cm^3), the extracts were dried, concentrated and the residue crystallized from the mixture benzene—hexane (5:1). Yield 0.48 g (66.3%) of compound *20*, m.p. 83°C.

For $C_{30}H_{31}NO_7$ (517.6) calculated: 69.62% C, 6.04% H, 2.70% N; found: 69.41% C, 5.92% H, 2.63% N. UV spectrum, λ_{max}^{MeOH}/nm (log ε): 225 (4.86), 314 (3.75), λ_{min}^{MeOH}/nm (log ε): 296 (3.66). IR spectrum, cm^{-1}: 1690, 1620, 1495, 1270, 1085, 1050. ^{1}H-NMR spectrum ($CDCl_3$), δ/p.p.m.: 7.42—7.00 (m, 5H) H_{arom}; 6.70 (d, 1H), 5.80 (d, 1H), ABq, $H_{6'}H_{7'}$, $J_{6',7'}$ 8 Hz; 6.27 (s, 1H) H_7; 5.92 (s, 2H) OCH_2O; 4.43 (s, 2H) $NCH_2C_6H_5$; 4.70 (m, 1H) H_1; 3.75 (s, 1H) H_3; 4.03 (s, 3H), 3.98 (s, 3H), 3.83 (s, 3H) 3 × OCH_3; 3.55 (q, 2H) OCH_2CH_3, J 5 Hz; 1.28 (t, 3H) OCH_2CH_3, J 5 Hz; 0.86 (d, 3H) C-1,CH_3, J 6 Hz.

(Z)-6,7-Dimethoxy-3,1'-(8'-methoxy-2',2'-dimethyl-1',2',3',4'--tetrahydro-1,3-dioxolo[4,5-f]isoquinolylidenium)isoindolin-1-one bromide (21)

Compound *2* (1.5 g; 2.9 mmol) in methanol (300 cm^3) was exposed to the daylight for 5 days, methanol was evaporated, the residue crystallized from the mixture ethanol—water (1 : 1), the crystals of the unreacted portion of *2* filtered off and the filtrate was concentrated *in vacuo* and by crystallization from benzene 0.068 g of compound *21* was obtained, m.p. 228—232°C.

For $C_{23}H_{25}N_2O_6^+Br^-$ (505.4) calculated: 54.66% C, 4.99% H, 5.54% N; found: 54.52% C, 4.81% H, 5.46% N. UV spectrum, λ_{max}/nm (log ε): 384 (4.13), λ_{min}/nm (log ε): 298 (3.65) (in ethanol); λ_{max}/nm (log ε): 375 (4.15), λ_{min}/nm (log ε): 292 (3.61) (in 0.01 M ethanolic HCl); λ_{max}/nm (log ε): 397 (4.15), λ_{min}/nm (log ε): 292 (3.61) (in 0.01 M ethanolic KOH). IR spectrum, cm^{-1}: 3450, 1640, 1600, 1480, 1270, 1080, 1050. ^{1}H-NMR spectrum ($CDCl_3$), δ/p.p.m.: 6.69 (d, 1H), 6.53 (d, 1H), ABq, H_4H_5, $J_{4,5}$ 8 Hz; 6.67 (s, 1H) H_5; 6.00 (s, 2H) OCH_2O; 3.87 (s, 3H), 3.73 (s, 3H), 3.50 (s, 3H) 3 × OCH_3; 3.16—2.75 (m, 4H) CH_2CH_2; 2.50 (s, 6H) $N(CH_3)_2$. Mass spectrum, m/z (relative intensity, %): 425 (43), 410 (71), 381 (51), 380 (100), 379 (71), 366 (46), 364 (38), 336 (21), 308 (16).

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