5*H*-Isoindolo[1,2-*b*][3]benzazepines
VII.* Cyclization of *N*-substituted derivatives of narceone imide

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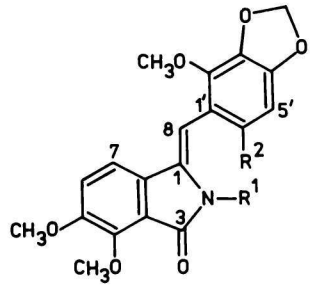
Received 12 April 1989

Narceone imide, prepared from the secophthalideisoquinoline alkaloid narceine imide, was alkoxycarbonyl-methylated with esters of bromoacetic or iodoacetic acid. The (*E*,*Z*)-butoxycarbonylmethyl narceone imide cyclized to 2-methoxycarbonylmethyl-1′-methyl-5′,6′-methylenedioxy-6,7,3′,4′-tetramethoxyisoindoline-3-spiro-2′-indan-1-one. 1′-Methylene-5′,6′-methylenedioxy-3′-oxo-6,7,4′-trimethoxyisoindoline-3-spiro-2′-indan-1-one was obtained by addition of bromine followed by dehydrobromination and cyclization of narceone imide.

Our preceding papers [1—3] dealt with the synthesis of tetracyclic compounds starting from narceone imide (*II*), prepared from narceine imide (*I*), an alkaloid of the secophthalideisoquinoline group. All compounds, excepting those having an amino group capable to give salts with acids were water-insoluble. Of hydrophilic derivatives of narceine imide (*I*) narceine imide *N*-oxide exerted the highest activity against the P-388 leukemia cells, approximately 80-fold of that of the starting *I* [4]. The goal of this paper was to synthesize heterocyclic compounds with a substituted carboxymethyl group from compound *I* to obtain water-soluble salts required for biological tests.

Narceine imide gave on reaction with butyl iodoacetate in chloroform the ammonium salt *III*, which was cautiously hydrolyzed with dilute ethanolic KOH to the betaine *IV*; removal of the solvent and adjustment of the pH to 2.5 resulted in separation of the ammonium acid *V* A vigorous heating of the ammonium salt *III* led to formation of narceone imide (*II*). Another site suitable for attaching the carboxymethyl group to *I* is the imide nitrogen of the isoindoline moiety. To alkylate this position it is more favourable to start from narceone imide obtained by a Hofmann degradation of narceine imide iodomethylate [5].

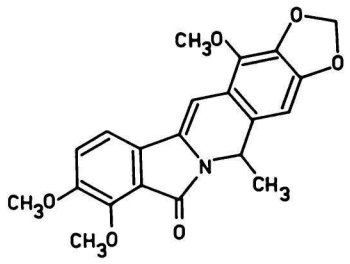
* For Part *VI* see *Chem. Papers 42*, 683 (1988).



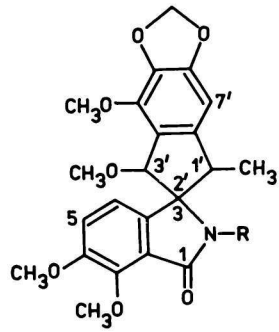
	R^1	R^2
I-Z	H	$CH_2CH_2N(CH_3)_2$
II-Z	H	$CH{=}CH^AH^B$
III-Z	H	$CH_2CH_2N^+(CH_3)_2CH_2COOC_4H_9$ I^-
IV-Z	H	$CH_2CH_2N^+(CH_3)_2CH_2COO^-$
V-Z	H	$CH_2CH_2N^+(CH_3)_2CH_2COOH$ Cl^-
VI-Z	$CH_2COOC_4H_9$	$CH{=}CH^AH^B$
VII-Z	CH_2COOH	$CH{=}CH^AH^B$
VIII-Z	$CH(CH_3)COOC_2H_5$	$CH{=}CH^AH^B$

Potassium salt of the imide *II* and butyl bromoacetate in dimethylformamide gave rise to the substituted narceone imide, which was according to thin-layer chromatography and high-pressure liquid chromatography a single compound. Nevertheless, the ^{1}H NMR spectrum showed this alkylation product to be a mixture of geometric isomers in a 72:28 ratio of *VI-E* to *VI-Z*. Crucial differences in the spectrum of these isomers showed positions of protons H-6 and H-7 at the aromatic ring appearing as an AB quartet at $\delta = 7.16$ and 7.48 for the *VI-Z* and, due to shielding of the benzylidene part by benzene ring, at $\delta = 6.60$ and 6.78 for the *VI-E* isomers. Remarkable differences were also seen in shifts of vinylic proton signals of the ethylidene bridge connecting benzene rings and methylene protons of the N-2—CH_2—CO grouping. The representation of *VI-E* and *VI-Z* isomers in the mixture was calculated from the intensities of peaks associated with H-5′ similarly as was done with the geometric isomers of narceine imide [6]. Hydrolysis of *VI-E*, *VI-Z* in methanolic KOH and acidification of the mixture afforded acid *VII* as a sole *Z*-isomer. A single geometric isomer *VIII-Z* was also isolated when reacting the imide *II* with ethyl 2-bromopropionate.

Narceone imide cyclized in strong mineral acids to a mixture of 5*H*-isoindolo[1,2-*b*]isoquinolone *IX* and isoindoline-3-spiro-2′-indan-1-one *X* [5]. Cyclization of *N*-substituted derivatives of narceone imide could yield compounds



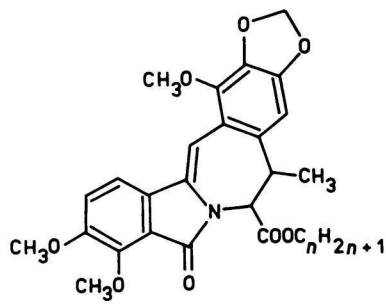
IX



X R = H

XII R = CH_2COOCH_3

XIV R = CH_2COOH



XI

of 7,8-dihydro-5*H*-isoindolo[1,2-*b*][3]benzazepine *XI*. The mixture *VI-E*, *VI-Z* furnished two compounds on heating in methanolic hydrochloric acid: *N*-methoxycarbonylmethylisoindoline-3-spiro-2′-indan-1-one *XII* and (*E*)-methoxycarbonylmethylnarceone imide *XIII-E*. Spatial arrangement of the former was deduced from the NOE experiment. Irradiation of the proton signal at $\delta = 5.93$ resulted in an intensity increase of that of the neighbouring proton ($\delta = 6.81$) and the alicyclic C-3′—H ($\delta = 4.47$) one. Irradiation of the proton signal at

$\delta = 6.81$ caused an intensity increase of those at $\delta = 5.93$ and 3.81 belonging to the group C-6—OCH_3. These data evidenced the signal at $\delta = 5.91$ to be attributed to H-4; signal for H-5 ($\delta = 6.81$) lay in a lower magnetic field. The

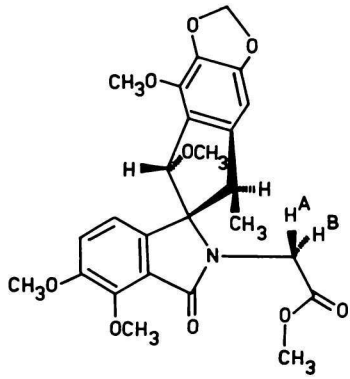
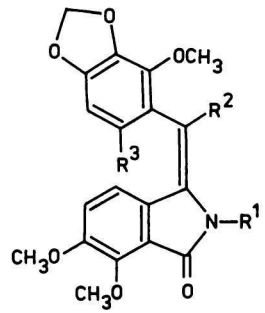


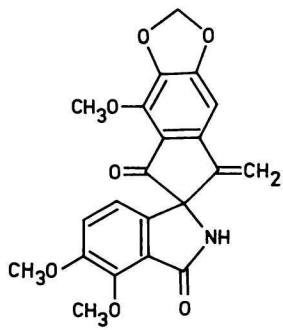
Fig. 1. Spatial arrangement of *XII*.



	R^1	R^2	R^3
VI–E	$CH_2COOC_4H_9$	H	$CH{=}CH^AH^B$
XIII–E	CH_2COOCH_3	H	$CH{=}CH^AH^B$
XV–Z	$CH_2COOC_4H_9$	Br	$CHBrCH_2Br$
XVI–Z	CH_2COOH	Br	$CBr{=}CH^AH^B$
XVII–Z	H	Br	$CHBrCH_2Br$
XVIII–Z	H	OCH_3	$C(OCH_3){=}CH^AH^B$

relative configuration of substituents of the alicyclic moiety of the indane backbone was derived from the intensity enhancement of the H-4 signal after irradiating the H-3′ and C-1′—CH_3 protons. Considering all these findings, the configuration shown in Fig. 1 was assigned to compound *XII*. Alkaline hydrolysis of *XII* and the following work-up gave *XIV*

Addition of two molecules of bromine to the double bonds of the mixture *VI-E*, *VI-Z* led to formation of a single tribromo derivative *XV-Z via* tetrabromonarceone imide and a spontaneous dehydrobromination already described with bromination of narceine imide [7]. Further dehydrobromination of *XV-Z* by KOH coupled with hydrolysis of the ester group and work-up gave acid *XVI-Z*, which did not cyclize in the presence of mineral acids. The imide *XVII-Z* [7] obtained by bromination of *II* underwent dehydrobromination in the side chain with sodium methanolate under a simultaneous replacement of bromine by methoxyl groups (*XVIII-Z*); heating of this compound in methanolic hydrochloric acid furnished *XIX*. The electron impact mass spectrum of this compound is quite simple; only intense peaks of the molecular radical ion



XIX

dominated the spectrum together with minor peaks belonging to M − 15 and M − 29 species. The ^{1}H NMR spectrum showed signals of three methoxyl groups, three protons at aromatic ring, two protons of one dioxymethylene grouping and one exocyclic methylene (δ = 5.62 and 5.21) with a corresponding signal at δ = 95.6 in the ^{13}C NMR spectrum. Relevant proofs for the structure assignment were afforded by the ^{13}C NMR spectrum with signals of the quaternary sp^3 carbon (δ = 71.2), ethylidene carbon (δ = 157.1), amide carbonyl (δ = 169.8) and another carbonyl carbon (δ = 193.6). These data allowed to ascribe to *XIX* the structure of 1′-methylene-5′,6′-methylenedioxy-3′-oxo-6,7,4′--trimethoxyisoindoline-3-spiro-2′-indan-1-one.

Experimental

Melting points were determined on a Kofler micro hot-stage. The IR and the EI-mass spectra were measured with Perkin—Elmer, model 983, and Jeol JMS 100D ($U = 70$ eV and $I = 300$ μA) apparatuses, respectively. The ^{1}H NMR spectra were recorded with a Bruker AM-300 spectrometer operating at the frequency 300 MHz. For HPLC 150 mm × 3 mm column packed with Separon SGX C18, 7 μm (Tessek, Prague), mobile phase methanol—water ($\varphi_r = 80:20$) were used at a flow rate 0.4 cm^3 min^{-1}, UV detector ($\lambda = 254$ nm). Silufol sheets UV 254 were employed for thin-layer chromatography; solvent systems: benzene—methanol $\varphi_r = 10:0.5$ (S_1), ether—hexane $\varphi_r = 1:1$ (S_2), benzene—methanol $\varphi_r = 9:1$ (S_3).

Reaction of narceine imide (I-Z) with butyl iodoacetate

Narceine imide (*I-Z*, 1 g; 2.35 mmol) in chloroform (50 cm^3) was stirred with butyl iodoacetate (0.7 g; 2.89 mmol) at room temperature. After 2 h the solvent was distilled off and the residue was crystallized from methanol—ether ($\varphi_r = 2:1$). Yield of *III-Z* was 1.18 g (75.2 %), m.p. = 208 °C. For $C_{29}H_{37}IN_2O_8$ ($M_r = 668.5$) w_i (calc.): 52.10 % C, 5.58 % H, 4.19 % N; w_i(found): 51.94 % C, 5.40 % H, 4.19 % N. IR spectrum (KBr), $\tilde{\nu}$/cm^{-1}: 3428 (ν(N—H)), 1744, 1696 (ν(C=O)), 1655 (ν(C=C)).

Compound *III-Z* (1.0 g; 1.5 mmol) was heated with methanolic KOH ($\varrho = 5$ g dm^{-3} 40 cm^3) for 45 min, the solvent was distilled off, the residue was dissolved in water, the pH of the solution was adjusted by addition of HCl ($\varrho = 6.3$ g dm^{-3}) to 2.5, the separated crystals were filtered off and recrystallized from methanol—water ($\varphi_r = 1:1$). Yield of *V-Z* was 0.48 g (61.6 %), m.p. = 228—230 °C (decomp.). For $C_{25}H_{29}ClN_2O_8$ ($M_r = 520.9$) w_i(calc.): 57.64 % C, 5.61 % H, 5.37 % N; w_i(found): 57.50 % C, 5.41 % H, 5.34 % N. IR spectrum (KBr), $\tilde{\nu}$/cm^{-1}: 3423 (ν(O—H)), (ν(N—H)), 1748 (ν(C=O)), 1695 (ν(C=O)), 1663 (ν(C=C)), 1498, 1453. ^{1}H NMR spectrum (CD_3OD), δ: 9.89 (s, 1H, COOH), 7.72, 7.34 (ABq, 2H, H-7, H-6, $J_{6,7} = 8.4$ Hz), 6.68 (s, 1H, H-5'), 6.32 (s, 1H, H-8), 6.01 (s, 2H, OCH_2O), 3.89, 3.88, 3.86 (3s, 3 × 3H, 3 × OCH_3), 3.56 (m, 2H, $CH_2\underline{CH_2}N$), 3.18 (s, 6H, $N(CH_3)_2$), 3.00 (m, 2H, $\underline{CH_2}CH_2N$).

2-Butoxycarbonylmethyl-4,5-dimethoxy-1-(6'-ethenyl-2'-methoxy-3',4'-methylenedioxybenzylidene)isoindolin-3-ones (VI-E, VI-Z)

Potassium *tert*-butoxide (0.51 g K; 13.1 mmol) was added to a solution of narceone imide (*II-Z*, 5.0 g; 13.12 mmol) in dimethylformamide (120 cm^3); after 1 h stirring butyl bromoacetate (2.73 g; 14 mmol) and finally, after 3 h stirring acetic acid (1 cm^3) were added. The solvents were removed under diminished pressure, the residue was dissolved in ether, filtered, the filtrate was concentrated, poured on an alumina-packed column eluted with ethyl acetate and chromatographed with ether—heptane ($\varphi_r = 1:2$) to afford the mixture *VI-E*, *VI-Z* (6.48 g, 66.1 %), $R_f = 0.54$ (S_1), m.p. = 156—158 °C. For

$C_{27}H_{29}NO_8$ (M_r = 495.5) w_i(calc.): 65.44 % C, 5.90 % H, 2.82 % N; w_i(found): 65.39 % C, 5.85 % H, 2.76 % N. IR spectrum ($CHCl_3$), $\tilde{\nu}$/cm^{-1}: 3026, 3000, 2955 (ν(O—H)), 1746, 1701 (ν(C=O)), 1657 (ν(C=C)), 1600, 1496, 1472. Mass spectrum, m/z (I_r/%): 495 (100), 480 (8), 467 (3), 464 (11), 439 (9), 394 (10), 393 (10), 366 (18), 365 (27), 350 (14), 306 (31). ^{1}H NMR spectrum ($CDCl_3$) for *VI-Z*, δ: 7.48, 7.16 (ABq, 2H, H-7, H-6, $J_{6,7}$ = 8.4 Hz), 6.79 (s, 1H, H-5′), 6.65 (dd, 1H, H-1″, $J_{1'',2''A}$ = 17.4 Hz, $J_{1'',2''B}$ = 10.9 Hz), 6.26 (s, 1H, H-8), 5.96 (ABq, 2H, OCH_2O, J = 1.5 Hz), 5.57 (dd, 1H, H^A-2″, $J_{2''A,B}$ = 1.0 Hz), 5.14 (dd, 1H, H^B-2″), 4.33, 4.30 (ABq, 2H, NCH_2CO, J = 17.4 Hz), 4.10, 3.96, 3.95 (3s, 3 × 3H, 3 × OCH_3), 3.85 (t, 2H, $COOCH_2CH_2$, J = 6.70 Hz), 1.42, 1.20 (m, 4H, $COOCH_2CH_2CH_2$), 0.85 (t, 3H, CH_2CH_3, J = 7.3 Hz). ^{1}H NMR spectrum ($CDCl_3$) for *VI-E*, δ: 6.89 (s, 1H, H-5′), 6.87, 6.60 (ABq, 2H, H-6, H-7, $J_{6,7}$ = 8.1 Hz), 6.73 (dd, 1H, H-1″, $J_{1'',2''A}$ = 17.5 Hz, $J_{1'',2''B}$ = 10.8 Hz), 5.98 (ABq, 2H, OCH_2O, J = 1.2 Hz), 5.85 (s, 1H, H-8), 5.52 (dd, 1H, H^B-2″, $J_{2''A,2''B}$ = 1.0 Hz), 5.02 (dd, 1H, H^A-2″), 4.80, 4.50 (ABq, 2H, NCH_2CO, J = 17.5 Hz), 4.18 (t, 2H, $COOCH_2$, J = 6.7 Hz), 4.07, 3.94, 3.84 (3s, 3 × 3H, 3 × OCH_3), 1.65, 1.37 (m, 2 × 2H, $COOCH_2CH_2CH_2$), 0.89 (t, 3H, CH_2CH_3, J = 7.3 Hz).

4,5-Dimethoxy-1-(6′-ethenyl-2′-methoxy-3′,4′-methylenedioxybenzylidene)--2-carboxymethylisoindolin-3-one (VII-Z)

The mixture of isomers *VI-E*, *VI-Z* (φ_r = 1:4; 0.5 g, 1.01 mmol) was heated with methanolic KOH (ϱ = 5.0 g dm^{-3}) for 30 min, the solvent was distilled off, the residue was dissolved in water, the pH was adjusted by addition of HCl to 1.5, the separated precipitate was filtered off and crystallized from chloroform—ethanol (φ_r = 2:1). Yield of *VII-Z* was 0.3 g (67.7 %), m.p. = 240—242 °C. For $C_{23}H_{21}NO_8$ (M_r = 439.4) w_i(calc.): 62.87 % C, 4.82 % H, 3.19 % N; w_i(found): 62.77 % C, 4.75 % H, 3.12 % N. ^{1}H NMR spectrum (DMSO-d_6), δ: 12.4 (s, 1H, COOH), 7.75, 7.38 (ABq, 2H, H-7, H-6, $J_{6,7}$ = 8.3 Hz), 6.96 (s, 1H, H-5′), 6.46 (s, 1H, H-8), 6.58 (dd, 1H, H-1″, $J_{1'',2''A}$ = 17.2 Hz, $J_{1'',2''B}$ = 10.9 Hz), 6.05 (s, 2H, OCH_2O), 5.68 (d, 1H, H^A-2″), 5.14 (d, 1H, H^B-2″), 4.18, 4.03 (ABq, 2H, NCH_2CO, J = 18.1 Hz), 3.93, 3.89, 3.87 (3s, 3 × 3H, 3 × OCH_3). Mass spectrum, m/z (I_r/%): 439 (100), 424 (6), 408 (12), 396 (34), 381 (32), 368 (42), 250 (16).

4,5-Dimethoxy-1-(6′-ethenyl-2′-methoxy-3′,4′-methylenedioxybenzylidene)--2-(1-ethoxycarbonyl-1-ethyl)isoindolin-3-one (VIII-Z)

Narceone imide (*II-Z*, 2 g; 5.2 mmol) was reacted with ethyl 2-bromopropionate (0.95 g; 5.3 mmol) by the same procedure as with the preparation of *VI-E*, *VI-Z*. Crystallization from ether-heptane (φ_r = 1:2) afforded 1.30 g (52 %) of *VIII-Z*, R_f = 0.85 (S_2), m.p. = 148—150 °C. For $C_{26}H_{27}NO_8$ (M_r = 481.5) w_i(calc.): 64.85 % C, 5.66 % H, 2.91 % N; w_i(found): 64.79 % C, 5.55 % H, 2.87 % N. ^{1}H NMR spectrum ($CDCl_3$), δ: 7.47, 7.02 (ABq, 2H, H-7, H-6, $J_{6,7}$ = 8.3 Hz), 6.86 (s, 1H, H-5′), 6.85 (s, 1H, H-8), 6.76 (dd, 1H, H-1″, $J_{1'',2''A}$ = 17.5 Hz, $J_{1'',2''B}$ = 10.9 Hz), 5.94 (ABq, 2H, OCH_2O, J = 1.2 Hz),

5.50 (q, 1H, NCH(CH$_3$)CO, J = 7.1 Hz), 5.48 (dd, 1H, H^A-2″, $J_{2''A,\,2''B}$ = 1.3 Hz), 5.00 (dd, 1H, H^B-2″), 4.12 (q, 2H, COOCH$_2$CH$_3$, J = 7.1 Hz), 4.01, 3.95, 3.92 (3s, 3 × 3H, 3 × OCH$_3$), 1.64 (d, 3H, CHCH$_3$, J = 7.10 Hz), 1.16 (t, 3H, CH$_2$CH$_3$, J = 7.1 Hz). Mass spectrum, m/z (I_r/%): 481 (4), 436 (1.5), 381 (100), 366 (6), 365 (6), 350 (5), 191 (5).

Cyclization of isomers VI-E, VI-Z

The mixture of *VI-E, VI-Z* (1 g; 2 mmol) dissolved in methanol (100 cm^3) containing sulfuric acid (0.2 cm^3) was heated for 24 h, cooled, neutralized with aqueous solution of NaHCO$_3$, methanol was distilled off, the residue was extracted with chloroform, the solvent was removed and the residue was chromatographed on a silica gel packed column with heptane—ethyl acetate (gradient elution), the fractions were checked by HPLC. Fractions *4—8* were combined, the solvent was distilled off and the residue was crystallized from ether—methanol (φ_r = 1:1) to give 0.148 g (32.6 %) of *XIII-E*, R_f = 0.62 (S$_3$), m.p. = 174—176 °C. For $C_{24}H_{23}NO_8$ (M_r = 453.4) w_i(calc.): 63.57 % C, 5.11 % H, 3.08 % N; w_i(found): 63.52 % C, 5.01 % H, 3.02 % N. ^{1}H NMR spectrum (CDCl$_3$), δ: 6.89, 6.60 (ABq, 2H, H-6, H-7, $J_{6,7}$ = 8.4 Hz), 6.87 (s, 1H, H-5′), 6.73 (dd, 1H, H-1″, $J_{1''\,2''A}$ = 17.5 Hz, $J_{1'',2''B}$ = 11.0 Hz), 6.00 (ABq, 2H, OCH$_2$O, J = 1.5 Hz), 5.85 (s, 1H, H-8), 5.53 (d, 1H, H^A-2″), 5.04 (d, 1H, H^B-2″), 4.80, 4.57 (ABq, 2H, NCH$_2$CO, J = 17.7 Hz), 4.06, 3.88, 3.84, 3.79 (4s, 4 × 3H, 4 × OCH$_3$). Mass spectrum, m/z (I_r/%): 453 (100), 438 (8), 422 (12), 393 (3), 380 (6), 366 (9), 263 (17).

Combined fractions *10—15* gave on crystallization from methanol compound *XII* (0.515 g, 54 %), R_f = 0.51 (S$_3$), m.p. = 162—164 °C. For $C_{25}H_{27}NO_9$ (M_r = 485.5) w_i(calc.): 61.85 % C, 5.61 % H, 2.88 % N; w_i(found): 61.77 % C, 5.55 % H, 2.79 % N. IR spectrum (CHCl$_3$), $\tilde{\nu}$/cm^{-1}: 3082, 3047, 2992 (ν(C—H)), 1753 (ν(C=O)), 1689 (ν(CO$_{amide}$)), 1620, 1528. ^{1}H NMR spectrum (CDCl$_3$), δ: 6.81, 5.93 (ABq, 2H, H-4, H-5, $J_{4,5}$ = 8.4 Hz), 6.45 (s, 1H, H-7′), 5.98 (ABq, 2H, OCH$_2$O, J = 1.5 Hz), 4.47 (s, 1H, H-3′), 4.66, 4.36 (ABq, 2H, NCH$_2$CO, J = 17.2 Hz), 4.09 (s, 3H, C-7—OCH$_3$), 4.02 (s, 3H, C-4′—OCH$_3$), 3.81 (s, 3H, C-6—OCH$_3$), 3.79 (q, 1H, H-1′, $J_{1'\,CH_3}$ = 7.0 Hz), 3.78 (s, 3H, COOCH$_3$), 3.29 (s, 3H, C-3′—OCH$_3$). 0.80 (d, 3H, C-1′—CH$_3$). Mass spectrum, m/z (I_r/%): 485 (20), 470 (13), 453 (100), 438 (14), 395 (41), 380 (79), 264 (10).

A 30 min saponification of compound *XII* (0.2 g; 0.41 mmol) in methanolic KOH, removal of the solvent and acidification to pH 1.4 gave a precipitate, which was crystallized from methanol—water (φ_r = 1:1). Yield of *XIV* was 0.15 g (77.6 %), m.p. = 265—267 °C. For $C_{24}H_{25}NO_9$ (M_r = 471.5) w_i(calc.): 61.14 % C, 5.34 % H, 2.97 % N; w_i(found): 61.08 % C, 5.30 % H, 2.81 % N.

8-Bromo-4,5-dimethoxy-1-[6′-(1-bromoethenyl)-2′-methoxy-3′,4′--methylenedioxybenzylidene]-2-carboxymethylisoindolin-3-one (XVI-Z)

Bromine (0.87 g; 5.4 mmol) in chloroform (30 cm^3) was added to a stirred solution of *VI-E, VI-Z* (1.35 g; 2.72 mmol) in chloroform (50 cm^3) cooled to 5 °C. The reaction

mixture was concentrated after 15 min and the residue was separated on an alumina packed column by elution with ethyl acetate. Crystallization of the product from heptane—ethyl acetate ($\varphi_r = 1:1$) afforded *XV-Z* (1.75 g, 79 %), m.p. = 115—117 °C. For $C_{27}H_{28}Br_3NO_8$ ($M_r = 734.3$) w_i(calc.): 44.17 % C, 3.84 % H, 1.91 % N; w_i(found): 44.23 % C, 3.94 % H, 1.89 % N. IR spectrum ($CHCl_3$), $\tilde{\nu}/cm^{-1}$: 2999, 2939 (ν(C—H)), 1710 (ν(CO)), 1629, 1613 (ν(C=C)). ^{1}H NMR spectrum ($CDCl_3$), δ: 6.85, 6.81 (ABq, 2H, H-6, H-7, $J_{6,7} = 8.5$ Hz), 6.45 (s, 1H, H-5'), 6.10 (ABq, 2H, OCH_2O), 5.57 (m, 1H, CHBr), 5.20 (m, 1H, CH_2Br), 4.40 (m, 2H, NCH_2CO), 4.04, 3.97, 3.82 (3s, 3 × 3H, 3 × OCH_3). Mass spectrum, m/z (I_r/%): 652 (1), 654 (2), 656 (1), 574 (43), 572 (43), 494 (80), 493 (100).

Compound *XV-Z* (0.4 g; 0.54 mmol) was heated in methanolic KOH for 2 h, methanol was removed, the residue was dissolved in water and the pH was adjusted to 1.5. The separated precipitate was crystallized from methanol—water ($\varphi_r = 1:1$) to give *XVI-Z* (0.27 g, 84 %), m.p. = 207—209 °C (decomp.). For $C_{23}H_{19}Br_2NO_8$ ($M_r = 597.2$) w_i(calc.): 46.26 % C, 3.21 % H, 2.34 % N; w_i(found): 46.19 % C, 3.15 % H, 2.26 % N. Mass spectrum, m/z (I_r/%): 599 (1), 597 (2), 595 (1), 518 (2), 517 (2), 516 (2), 515 (2), 438 (100).

1'-Methylene-5',6'-methylenedioxy-3'-oxo-6,7,4'-trimethoxyisoindoline--3-spiro-2'-indan-1-one (XIX)

Tribromide *XVII-Z* (3 g; 4.8 mmol), prepared according to [4], was heated in methanolic sodium methoxide for 4 h; the solvent was distilled off and acetic acid ($\varrho = 10$ g dm^{-3}, 30 cm^3) was added to the residue. The separated precipitate was filtered and crystallized from ether to yield *XVIII-Z* (1.7 g, 80 %), m.p. = 254—256 °C. For $C_{23}H_{23}NO_8$ ($M_r = 441.4$) w_i(calc.): 62.58 % C, 5.25 % H, 3.17 % N; w_i(found): 62.47 % C, 5.18 % H, 3.15 % N. IR spectrum ($CHCl_3$), $\tilde{\nu}/cm^{-1}$: 3441 (ν(N—H)), 3131, 3066, 2938 (ν(C—H)), 1701 (ν(CO)), 1655 (ν(C=C)). Mass spectrum, m/z (I_r/%): 441 (40), 410 (100), 395 (13), 380 (7), 366 (6), 221 (2), 206 (5).

Compound *XVIII-Z* (1.2 g; 2.7 mmol) was heated in methanolic hydrochloric acid ($\varrho = 50$ g dm^{-3}) for 1 h, the solvent was evaporated, water was added to the residue, the separated precipitate was filtered off and crystallized from heptane—ethyl acetate ($\varphi_r = 2:1$). Compound *XIX* (0.8 g, 75 %) had m.p. = 260—262 °C. For $C_{21}H_{17}NO_7$ ($M_r = 395.3$) w_i(calc.): 63.80 % C, 4.33 % H, 3.54 % N; w_i(found): 63.90 % C, 4.23 % H, 3.42 % N. IR spectrum ($CHCl_3$), $\tilde{\nu}/cm^{-1}$: 3434 (ν(N—H)), 3034, 2991, 2945 (ν(C—H)), 1712 (ν(CO)), 1608, 1488. ^{1}H NMR spectrum ($CDCl_3$), δ: 6.90, 6.55 (ABq, 2H, H-4, H-5, $J_{4,5} = 8.2$ Hz), 6.90 (s, 1H, H-5'), 6.20 (s, 1H, NH), 6.12 (ABq, 2H, OCH_2O, $J = 1.2$ Hz), 5.62 (d, 1H, CH^AH^B, $J = 0.8$ Hz), 5.21 (d, 1H, CH^AH^B), 4.15, 4.12, 3.83 (3s, 3 × 3H, 3 × OCH_3). Mass spectrum, m/z (I_r/%): 395 (100), 380 (12), 366 (8).

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Translated by Z. Votický