Synthesis and Characterization of New 7-Substituted 6,14-Ethenomorphinane Derivatives: *N*-{5-[(5*α*,7*α*)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}arenamines

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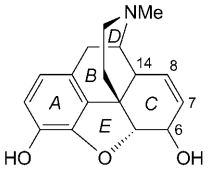
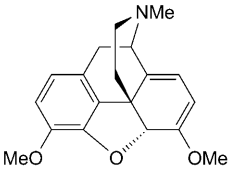
In this study, (5*α*,7*α*)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic acid hydrazide (**5**) was synthesized by the condensation of methyl (5*α*,7*α*)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylate (**4**) with $NH_2NH_2 \cdot H_2O$. The (5*α*,7*α*)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic acid 2-[(arylamino)carbonyl]hydrazides **6a**–**6q** were prepared by the reaction of **5** with corresponding substituted aryl isocyanates, and the *N*-{5-[(5*α*,7*α*)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}arenamines **7a**–**7q** were obtained *via* the cyclization reaction of **6a**–**6q** in the presence of $POCl_3$. The synthesized compounds have a rigid morphine structure, including the 6,14-*endo*-etheno bridge and the 5-(arylamino)-1,3,4-oxadiazol-2-yl residue at C(7) adopting the (*S*)-configuration (7*α*). The structures of the compounds were confirmed by high-resolution mass spectrometry (HR-MS) and various spectroscopic methods such as FT-IR, ^{1}H-NMR, ^{13}C-NMR, APT, and 2D-NMR (HETCOR, COSY, INADEQUATE).

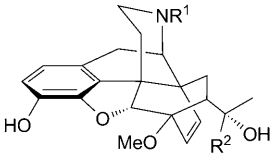
Introduction. – Thebaine (=(5*α*)-6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methylmorphinan; **2**) is one of the most important alkaloids which can be extracted from opium poppy (*Papaver somniferum*). Although thebaine cannot be used directly due to its toxic effect, its many semisynthetic derivatives have wide-ranging applications in pharmaceutical industry as narcotic analgesics and as pain-relief drugs [1][2]. For example, etorphine (**3a**), which is a thebaine derivative, is a well-known synthetic narcotic analgesic. Its analgesic activity is *ca.* 1000 times stronger than that of morphine (**1**), and it can be used in veterinary medicine [3]. Moreover, another important thebaine derivative, namely buprenorphine (**3b**), has some specific usage as a drug in narcotic overdosage, opioid abuse, and addiction [4]. The nature of the



Morphine (**1**)



Thebaine (**2**)



Etorphine (**3a**) R^1 = Me, R^2 = Pr
Buprenorphine (**3b**) R^1 = (cyclopropyl)CH_2, R^2 = ^{t}Bu

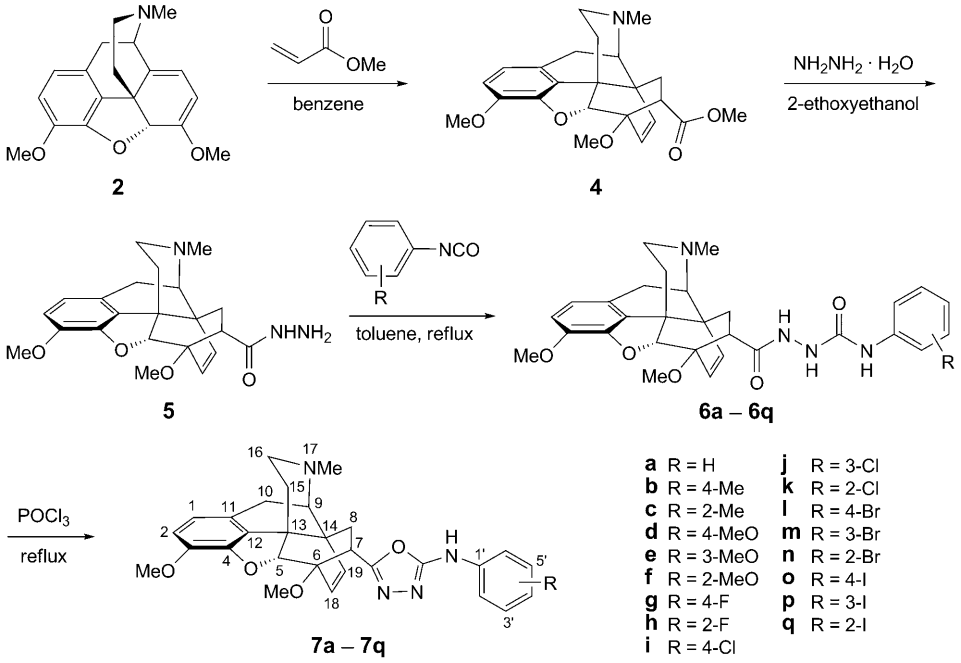
lipophilic substituents in α position of C(7) of the *C* ring and the 6,14-*endo*-etheno bridge in morphine alkaloids are significant factors for their analgesic activities [5]. Furthermore, essentially the *C* ring of such alkaloids affect their pharmacological properties [6]; hence, the synthesis and pharmacology of these compounds have been extensively studied. Opioids which are 7α-substituted 6,14-ethenomorphinan analogues are the main product of the *Diels–Alder* reaction of thebaine (**2**) with acrylates (= prop-2-enoates) or methyl vinyl ketone [7].

Also 1,3,4-oxadiazole derivatives display a broad spectrum of biological activities such as antimicrobial, antibacterial, analgesic, and antifungal activity and are thus of wide-ranging interest [8–11].

In this study, we report the synthesis and characterization of a series of novel 7-substituted 6,14-ethenomorphinans, *i.e.*, of *N*-{5-[(5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}arenamines (**7a–7q**), which are potential clinical analgesics.

Results and Discussion. – The synthesis of **7a–7q** from **2** *via* **4–6** is depicted in the *Scheme*. The structures of all compounds were established by IR, ^{1}H-NMR, ^{13}C-NMR, APT, and 2D-NMR spectroscopy, and by high-resolution mass spectrometry (HR-MS). All spectroscopic data were in accordance with the assigned structures. In addition, the crystal structure of compound **4** was previously reported by our group [12].

Scheme



The key intermediate in the present study is methyl (5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylate (=7α-(methoxycarbonyl)-6,7,8,14-tetrahydro-6,14-*endo*-ethenothebaine; **4**) which was prepared according to a previously described procedure [12]. The diene system of thebaine could potentially be attacked from both faces, yet reactions with dienophiles always occur from the same face due to steric hindrance of the N-bridge on the upper face. *Diels–Alder* reactions between thebaine and methyl acrylate predominantly give the (7α) adduct [7]. Thus, the configuration at C(7) of methyl carboxylate **4**, carboxylic acid hydrazide **5**, the 2-[(arylamino)carbonyl]hydrazides **6**, and the *N*-[5-(morphinan-7-yl)-1,3,4-oxadiazol-2-yl]arenamines **7** is (7*S*). Besides, the crystal structure of **4** reveals that it maintains the 'T' shape of the rigid morphine structure and contains a 6,14-etheno bridge (*Fig.*). This shape and this configuration were retained in all product of the described synthetic steps (see *Scheme*). The rigid structural and configurational features of morphine and related opioids are essential for the analgesic actions.

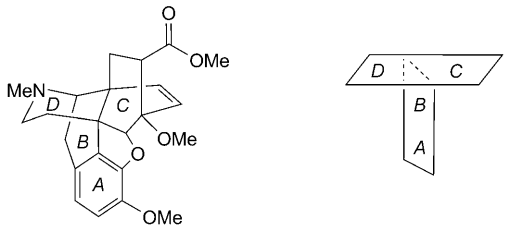


Figure. *'T' Shape of the rigid morphine structure*

Compound **5** was produced from the reaction of **4** with $NH_2NH_2 \cdot H_2O$ [13]. The ^{1}H-NMR spectra of **5** displayed no signals originating from the ester group; instead, new signals derived from the hydrazide structure appeared at δ 4.07 (NHNH_2) and 8.75 (N*H*NH_2). The reaction of carbohydrazide **5** with various aryl isocyanates gave (5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic acid 2-[(arylamino)carbonyl]hydrazides **6a–6q**. The IR spectra of compounds **6a–6q** showed two C=O absorption bands between 1709 and 1661 cm^{-1}; the ^{13}C-NMR signal of these groups were also observed. In addition, the ^{1}H-NMR spectra displayed three *s*s due to three different NH groups each integrating for one H-atom. On heating in $POCl_3$, **6a–6q** underwent smooth cyclization through dehydration to afford the *N*-{5-[(5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}arenamines **7a–7q**. The ^{1}H-NMR spectra of **7a–7q** displayed only one signal for an NH group integrating for one H-atom. In addition, the *endo*-orientation of the etheno bridge was confirmed by the considerable difference in the chemical shifts of H–C(18) and H–C(19), and also by the coupling between H–C(5) and H–C(18) in addition to that between H–C(7) and H–C(18) (*W*-shaped position of the bonds). As a result of the cyclization reactions upfield shifts of the resonances of H_β–C(7) were observed. In the ^{13}C-NMR spectra of **7a–7q**, no signal for a C=O group was detected.

In summary, we have synthesized a novel series of 7-[5-(arylamino)-1,3,4-oxadiazol-2-yl)-substituted (5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-etheno-morphinan derivatives as potential narcotic analgesics which are analogs of morphine.

Further work is in progress in our laboratory to evaluate the analgesic activity of these compounds.

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Experimental Part

General. All the reagents for syntheses were commercially available and used without further purification or purified by standard methods prior to use. Compounds **4** and **5** were synthesized by published methods [12][13]. TLC: *Silufol UV-254* plates. Column chromatography (CC): silica gel (SiO_2). M.p.: *Electrothermal-9100* apparatus; uncorrected. FT-IR Spectra: *Mattson-1000* spectrometer; KBr pellets; $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Bruker-400* NMR spectrometer; at 400 (^1H) and 100 MHz (^{13}C); in (D_6)DMSO; δ in ppm rel. to Me_4Si as internal standard, J in Hz. MS: *Waters-LCT-Premier-XE-LTOF* (TOF-MS) instruments; in m/z (rel. %). All the physical and spectroscopic data were in line with the previously reported results [12][13].

Compounds **6a**–**6q**: *General Procedure.* A mixture of (5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic acid hydrazide (1 mmol; **5**) and 1 mol-equiv. of the corresonding aryl isocyanate in toluene was heated at 70° for 2 h (TLC control). After evaporation of the toluene, a solid appeared which was recrystallized from an appropriate solvent to afford the desired compound.

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-[(Phenylamino)carbonyl]hydrazide (**6a**): Recrystallization from DMSO/H_2O. Yield 0.424 g (82%). M.p. 147–148°. IR: 3343*w*, 3319*w*, 3066*w*, 2971*m*, 1701*s*, 1696*s*, 1587*w*. ^{1}H-NMR: 9.67 (*s*, NH); 8.33 (br., NH); 8.18 (*s*, NH); 7.42 (*d*, *J*(2′,3′) = 7.7, H–C(2′,6′)); 6.95–7.29 (*m*, H–C(3′,5′), H–C(4′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.52 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.59 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.46 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.61 (*s*, H_β–C(5)); 3.71 (*s*, MeO–C(3)); 3.48 (*s*, MeO–C(6)); 3.18 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.12 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.50–2.88 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.42 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.3, H_α–C(10)); 2.31 (*s*, MeN); 1.75–2.20 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.32 (*dd*, *J*(8α,8β) = 12.6, *J*(7β,8α) = 5.7, H_α–C(8)). ^{13}C-NMR: 22.2 (C(10)); 30.9 (C(8)); 33.5 (C(15)); 40.7 (C(7)); 43.1 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.3 (*Me*O–C(6)); 56.5 (*Me*O–C(3)); 59.6 (C(9)); 81.3 (C(6)); 92.7 (C(5)); 113.8 (C(2)); 118.8 (C(2′,6′)); 119.8 (C(1)); 122.5 (C(4′)); 127.1 (C(18)); 128.8 (C(12)); 129.2 (C(3′,5′)); 134.3 (C(11)); 135.3 (C(19)); 139.9 (C(1′)); 141.6 (C(3)); 148.0 (C(4)); 155.7 (C=O); 171.9 (C=O). HR-MS: 517.2450 ($[M+H]^+$, $C_{29}H_{33}N_4O_5^+$; calc. 517.2451).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(4-Methylphenyl)amino]carbonyl}hydrazide (**6b**): Recrystallization from AcOEt/hexane. Yield 0.366 g (69%). M.p. 149–150°. IR: 3512*w*, 3365*w*, 3272*w*, 3062*w*, 2974*s*, 1692*s*, 1671*s*, 1641*m*, 1633*m*. ^{1}H-NMR: 9.67 (*s*, NH); 8.24 (br., NH); 8.14 (*s*, NH); 7.35 (*d*, *J*(2′,3′) = 8.3, H–C(2′,6′)); 7.07 (*d*, *J*(2′,3′) = 8.3, H–C(3′,5′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.52 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.58 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.46 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.61 (*s*, H_β–C(5)); 3.71 (*s*, MeO–C(3)); 3.51 (*s*, MeO–C(6)); 3.18 (*d*, *J*(9α,10α) = 6.2, H_α–C(9)); 3.12 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.50–2.88 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.42 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.4, H_α–C(10)); 2.30 (*s*, MeN); 2.23 (*s*, Me–C(4′)); 1.75–2.26 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.30 (*dd*, *J*(8α,8β) = 11.9, *J*(7β,8α) = 5.8, H_α–C(8)). ^{13}C-NMR: 20.8 (*Me*–C(4′)); 22.2 (C(10)); 30.8 (C(8)); 33.5 (C(15)); 40.9 (C(7)); 43.0 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.3 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.5 (C(9)); 81.3 (C(6)); 92.7 (C(5)); 113.7 (C(2)); 118.9 (C(2′,6′)); 119.8 (C(1)); 127.1 (C(18)); 128.8 (C(12)); 129.6 (C(3′,5′)); 131.3 (C(4′)); 134.3 (C(11)); 135.3 (C(19)); 137.3 (C(1′)); 141.6 (C(3)); 148.0 (C(4)); 155.7 (C=O); 172.0 (C=O). HR-MS: 531.2638 ($[M+H]^+$, $C_{30}H_{35}N_4O_5^+$; calc. 531.2607).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(2-Methylphenyl)amino]carbonyl}hydrazide (**6c**). Recrystallization from DMSO/H_2O. Yield 0.317 g (70%). M.p. 180–181°. IR: 3451*w*, 3384*w*, 3216*w*, 3060*w*, 2967*m*, 1704*s*, 1676*s*, 1637*m*, 1603*m*. ^{1}H-NMR: 9.80 (*s*, NH); 8.95 (*s*, NH); 7.75 (*s*, NH); 7.06–7.65 (*m*, H–C(3′), H–C(4′), H–C(5′), H–C(6′)); 6.68 (*d*, *J*(1,2) = 8.2,

H–C(2)); 6.57 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.68 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.52 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.61 (*s*, H_β–C(5)); 3.75 (*s*, MeO–C(3)); 3.49 (*s*, MeO–C(6)); 3.22 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.17 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.54–2.96 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.47 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.4, H_α–C(10)); 2.35 (*s*, MeN); 2.23 (*s*, Me–C(2′)); 1.80–2.30 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.30 (*dd*, *J*(8α,8β) = 12.0, *J*(7β,8α) = 6.2, H_α–C(8)). ^{13}C-NMR: 18.1 (*Me*–C(2′)); 22.2 (C(10)); 31.2 (C(8)); 33.5 (C(15)); 41.2 (C(7)); 43.0 (C(14)); 43.5 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.4 (*Me*O–C(6)); 56.5 (*Me*O–C(3)); 59.6 (C(9)); 81.1 (C(6)); 93.2 (C(5)); 113.9 (C(2)); 119.8 (C(1)); 123.7 (C(5′)); 126.5 (C(4′)); 127.0 (C(18)); 127.2 (C(2′)); 128.8 (C(12)); 130.6 (C(3′)); 134.2 (C(6′)); 134.3 (C(11)); 135.3 (C(19)); 137.5 (C(1′)); 141.6 (C(3)); 148.1 (C(4)); 156.0 (C=O); 171.8 (C=O). HR-MS: 531.2607 ($[M+H]^+$, $C_{30}H_{35}N_4O_5^+$; calc. 531.2607).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(4-Methoxyphenyl)amino]carbonyl}hydrazide (**6d**). Recrystallization from EtOH. Yield 0.431 g (81%). M.p. 144–145°. IR: 3501*w*, 3396*w*, 3285*w*, 3066*w*, 2980*m*, 1696*s*, 1687*s*, 1625*m*, 1600*m*. ^{1}H-NMR: 9.67 (*s*, NH); 8.17 (br., NH); 8.11 (*s*, NH); 7.31 (*d*, *J*(2′,3′) = 8.3, H–C(2′,6′)); 6.68 (*d*, *J*(2′,3′) = 8.3, H–C(3′,5′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.52 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.59 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.46 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.61 (*s*, H_β–C(5)); 3.71 (*s*, MeO–C(3), MeO–C(4′)); 3.51 (*s*, MeO–C(6)); 3.19 (*d*, *J*(9α,10α) = 6.2, H_α–C(9)); 3.12 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.51–2.87 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.43 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.2, H_α–C(10)); 2.30 (*s*, MeN); 1.75–2.28 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.30 (*dd*, *J*(8α,8β) = 11.5, *J*(7β,8α) = 5.6, H_α–C(8)). ^{13}C-NMR: 22.3 (C(10)); 30.8 (C(8)); 33.5 (C(15)); 40.9 (C(7)); 43.0 (C(14)); 43.5 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.4 (*Me*O–C(6)); 55.6 (*Me*O–C(4′)); 56.4 (*Me*O–C(3)); 59.5 (C(9)); 81.3 (C(6)); 92.8 (C(5)); 113.7 (C(2)); 114.4 (C(2′,6′)); 119.8 (C(1)); 120.6 (C(3′,5′)); 127.1 (C(18)); 128.8 (C(12)); 134.3 (C(1′)); 134.4 (C(11)); 135.4 (C(19)); 141.6 (C(3)); 148.0 (C(4)); 155.0 (C(4′)); 155.7 (C=O); 172.0 (C=O). HR-MS: 547.2563 ($[M+H]^+$, $C_{30}H_{35}N_4O_6^+$; calc. 547.2557).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(3-Methoxyphenyl)amino]carbonyl}hydrazide (**6e**). Recrystallization from EtOH. Yield 0.427 g (78%). M.p. 202–203°. IR: 3522*w*, 3471*w*, 3269*w*, 3053*w*, 2973*m*, 1692*s*, 1661*s*, 1641*m*, 1591*w*. ^{1}H-NMR: 9.73 (*s*, NH); 8.41 (br., NH); 8.24 (*s*, NH); 6.62–7.24 (*m*, H–C(2′), H–C(4′), H–C(5′), H–C(6′)); 6.68 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.58 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.62 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.51 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.66 (*s*, H_β–C(5)); 3.76 (*s*, MeO–C(3), MeO–C(3′)); 3.57 (*s*, MeO–C(6)); 3.23 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.17 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.56–2.94 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.47 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.3, H_α–C(10)); 2.36 (*s*, MeN); 1.81–2.30 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.36 (*dd*, *J*(8α,8β) = 11.8, *J*(7β,8α) = 5.8, H_α–C(8)). ^{13}C-NMR: 22.2 (C(10)); 31.2 (C(8)); 33.5 (C(15)); 40.9 (C(7)); 43.0 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.3 (*Me*O–C(6)); 55.4 (*Me*O–C(3′)); 56.4 (*Me*O–C(3)); 59.5 (C(9)); 81.2 (C(6)); 92.7 (C(5)); 104.7 (C(2′)); 107.7 (C(4′)); 111.1 (C(6′)); 113.7 (C(2)); 119.8 (C(1)); 127.1 (C(18)); 128.8 (C(12)); 130.0 (C(5′)); 134.3 (C(11)); 135.4 (C(19)); 141.1 (C(1′)); 141.6 (C(3)); 148.0 (C(4)); 155.6 (C=O); 160.1 (C(3′)); 171.9 (C=O). HR-MS: 547.2575 ($[M+H]^+$, $C_{30}H_{35}N_4O_6^+$; calc. 547.2557).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(2-Methoxyphenyl)amino]carbonyl}hydrazide (**6f**). Recrystallization from $CHCl_3$/hexane. Yield 0.410 g (75%). M.p. 204–205°. IR: 3478*w*, 3371*w*, 3212*w*, 3046*w*, 2960*m*, 1709*s*, 1678*s*, 1630*m*, 1594*m*. ^{1}H-NMR: 9.69 (*s*, NH); 8.63 (*s*, NH); 7.92 (*s*, NH); 8.01 (*d*, *J*(3′,4′) = 8.0, H–C(3′)); 7.00 (*d*, *J*(5′,6′) = 8.4, H–C(6′)); 6.87–6.93 (*m*, H–C(4′), H–C(5′)); 6.62 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.51 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.64 (*d*, *J*(18,19) = 8.8, H–C(18)); 5.43 (*d*, *J*(18,19) = 8.8, H–C(19)); 4.60 (*s*, H_β–C(5)); 3.82 (*s*, MeO–C(2′)); 3.76 (*s*, MeO–C(3)); 3.52 (*s*, MeO–C(6)); 3.17 (*d*, *J*(9α,10α) = 6.4, H_α–C(9)); 3.12 (*d*, *J*(10α,10β) = 18.8, H_β–C(10)); 2.30–2.92 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.42 (*dd*, *J*(10α,10β) = 18.5, *J*(9α,10α) = 6.4, H_α–C(10)); 2.30 (*s*, MeN); 1.75–2.28 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.26 (*dd*, *J*(8α,8β) = 12.0, *J*(7β,8α) = 6.2, H_α–C(8)). ^{13}C-NMR: 21.7 (C(10)); 31.2 (C(8)); 33.0 (C(15)); 40.7 (C(7)); 42.6 (C(14)); 43.6 (MeN); 45.0 (C(16)); 46.5 (C(13)); 52.3 (*Me*O–C(6)); 55.5 (*Me*O–C(2′)); 56.0 (*Me*O–C(3)); 59.1 (C(9)); 80.2 (C(6)); 92.6 (C(5)); 110.6 (C(3′)); 113.4 (C(2)); 118.6 (C(5′)); 119.3 (C(1)); 120.4 (C(6′)); 121.9 (C(4′)); 124.3 (C(1′)); 126.8 (C(18)); 128.3 (C(12)); 133.8 (C(11)); 141.1 (C(3)); 147.3 (C(2′)); 147.6 (C(4)); 134.4 (C(19)); 155.0 (C=O); 171.5 (C=O). HR-MS: 547.2549 ($[M+H]^+$, $C_{30}H_{35}N_4O_6^+$; calc. 547.2557).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(4-Fluorophenyl)amino]carbonyl}hydrazide (**6g**). Recrystallization from $CHCl_3$/hexane. Yield 0.391 g (73%). M.p. 144–145°. IR: 3397*w*, 3290*w*, 3247*w*, 3061*w*, 2933*m*, 1714*s*, 1671*s*, 1612*m*, 1604*m*. ^{1}H-NMR: 9.67 (*s*, NH); 8.38 (br., NH); 8.21 (*s*, NH); 6.62–7.24 (*m*, H–C(2′,6′), H–C(3′,5′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.52 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.61 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.45 (*d*, *J*(18,19) = 8.8, H–C(19)); 4.60 (*s*, H_β–C(5)); 3.78 (*s*, MeO–C(3)); 3.51 (*s*, MeO–C(6)); 3.19 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.13 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.50–2.91 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.41 (*dd*, *J*(10α,10β) = 18.5, *J*(9α,10α) = 6.3, H_α–C(10)); 2.33 (*s*, MeN); 1.76–2.25 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.31 (*dd*, *J*(8α,8β) = 11.6, *J*(7β,8α) = 5.8, H_α–C(8)). ^{13}C-NMR: 21.7 (C(10)); 30.4 (C(8)); 33.0 (C(15)); 40.5 (C(7)); 42.6 (C(14)); 43.1 (MeN); 45.0 (C(16)); 46.6 (C(13)); 51.8 (*Me*O–C(6)); 56.0 (*Me*O–C(3)); 59.0 (C(9)); 80.8 (C(6)); 92.3 (C(5)); 113.3 (C(2)); 115.1–115.3 (*J*(C(3′),F) = 22.1, C(3′)); 119.3 (C(1)); 120.1 (*J*(C(2′),F) = 7.4, C(2′)); 126.6 (C(18)); 128.3 (C(12)); 134.8 (C(11)); 134.9 (C(19)); 135.8 (C(1′)); 141.2 (C(3)); 147.5 (C(4)); 155.3 (C=O); 156.2–158.6 (*J*(C(4′),F) = 236.6, C(4′)); 171.4 (C=O). HR-MS: 535.2369 ($[M+H]^+$, $C_{29}H_{32}FN_4O_5^+$; calc. 535.2357).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(2-Fluorophenyl)amino]carbonyl}hydrazide (**6h**). Recrystallization from EtOH. Yield 0.433 g (81%). M.p. 134–135°. IR: 3371*w*, 3278*w*, 3215*w*, 3045*w*, 2938*w*, 1694*s*, 1680*s*, 1622*m*, 1611*m*. ^{1}H-NMR: 9.74 (*s*, NH); 8.49 (br., NH); 8.41 (*s*, NH); 6.99–7.97 (*m*, H–C(3′), H–C(4′), H–C(5′), H–C(6′)); 6.62 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.52 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.62 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.45 (*d*, *J*(18,19) = 8.8, H–C(19)); 4.56 (*s*, H_β–C(5)); 3.77 (*s*, MeO–C(3)); 3.47 (*s*, MeO–C(6)); 3.17 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.13 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.48–2.92 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.42 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.3, H_α–C(10)); 2.30 (*s*, MeN); 1.74–2.24 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.28 (*dd*, *J*(8α,8β) = 11.9, *J*(7β,8α) = 6.0, H_α–C(8)). ^{13}C-NMR: 22.2 (C(10)); 31.3 (C(8)); 33.5 (C(15)); 41.1 (C(7)); 43.0 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.3 (*Me*O–C(6)); 56.5 (*Me*O–C(3)); 59.6 (C(9)); 80.1 (C(6)); 93.0 (C(5)); 113.8 (C(2)); 115.4 (C(6′)); 115.4–115.6 (*J*(C(3′),F) = 19.4, C(3′)); 119.8 (C(1)); 123.4 (C(5′); 124.9 (*J*(C(4′),F) = 3.7, C(4′)); 127.1 (C(18)); 127.6–127.7 (*J*(C(1′),F) = 11.0, C(1′)); 128.8 (C(12)); 129.0–132.6 (*J*(C(2′),F) = 356.2, C(2′)); 134.3 (C(11)); 135.1 (C(19)); 141.6 (C(3)); 148.1 (C(4)); 155.4 (C=O); 171.9 (C=O). HR-MS: 535.2332 ($[M+H]^+$, $C_{29}H_{32}FN_4O_5^+$; calc. 535.2357).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(4-Chlorophenyl)amino]carbonyl}hydrazide (**6i**). Recrystallization from EtOH/$CHCl_3$. Yield 0.391 g (71%). M.p. 154–155°. IR: 3346*w*, 3252*w*, 3063*w*, 2963*m*, 1703*s*, 1662*s*, 1627*m*, 1598*m*. ^{1}H-NMR: 9.70 (*s*, NH); 8.51 (br., NH); 8.29 (*s*, NH); 7.45 (*d*, *J*(2′,3′) = 8.8, H–C(2′,6′)); 7.32 (*d*, *J*(2′,3′) = 8.8, H–C(3′,5′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.52 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.59 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.46 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.61 (*s*, H_β–C(5)); 3.71 (*s*, MeO–C(3)); 3.52 (*s*, MeO–C(6)); 3.18 (*d*, *J*(9α,10α) = 6.1, H_α–C(9)); 3.12 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.50–2.88 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.40 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.3, H_α–C(10)); 2.30 (*s*, MeN); 1.75–2.24 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.32 (*dd*, *J*(8α,8β) = 11.8, *J*(7β,8α) = 5.6, H_α–C(8)). ^{13}C-NMR: 22.2 (C(10)); 30.8 (C(8)); 33.5 (C(15)); 40.9 (C(7)); 43.0 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.3 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.5 (C(9)); 81.3 (C(6)); 92.6 (C(5)); 113.7 (C(2)); 119.8 (C(1)); 120.3 (C(2′)); 126.0 (C(4′)); 127.1 (C(18)); 128.8 (C(12)); 129.1 (C(3′)); 134.3 (C(11)); 135.3 (C(19)); 138.9 (C(1′)); 141.6 (C(3)); 147.9 (C(4)); 155.6 (C=O); 172.0 (C=O). HR-MS: 551.2042 ($[M+H]^+$, $C_{29}H_{32}ClN_4O_5^+$; calc. 551.2061).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(3-Chlorophenyl)amino]carbonyl}hydrazide (**6j**). Recrystallization from EtOH. Yield 0.485 g (88%). M.p. 142–143°. IR: 3471*w*, 3272*w*, 3050*w*, 2976*m*, 1698*s*, 1683*s*, 1637*m*, 1613*w*. ^{1}H-NMR: 9.69 (*s*, NH); 8.61 (br., NH); 8.34 (*s*, NH); 7.69 (*s*, H–C(2′)); 7.25–7.31 (*m*, H–C(4′), H–C(5′)); 7.01 (*d*, *J*(5′,6′) = 8.2, H–C(6′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.52 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.62 (*d*, *J*(18,19) = 8.8, H–C(18)); 5.51 (*d*, *J*(18,19) = 8.8, H–C(19)); 4.60 (*s*, H_β–C(5)); 3.71 (*s*, MeO–C(3)); 3.50 (*s*, MeO–C(6)); 3.20 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.13 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.51–2.89 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.42 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.3, H_α–C(10)); 2.31 (*s*, MeN); 1.75–2.24 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.30 (*dd*, *J*(8α,8β) = 11.8, *J*(7β,8α) = 5.8, H_α–C(8)). ^{13}C-NMR: 22.2 (C(10)); 30.8 (C(8)); 33.5 (C(15)); 41.0 (C(7)); 43.0 (C(14)); 43.6 (MeN);

45.5 (C(16)); 47.1 (C(13)); 52.3 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.5 (C(9)); 81.2 (C(6)); 92.7 (C(5)); 113.8 (C(2)); 117.2 (C(6′)); 118.1 (C(5′)); 119.8 (C(1)); 122.1 (C(4′)); 128.8 (C(12)); 130.9 (C(2′)); 133.6 (C(3′)); 134.3 (C(11)); 141.5 (C(1′)); 141.6 (C(3)); 148.0 (C(4)); 127.2 (C(18)); 135.3 (C(19)); 155.5 (C=O); 172.0 (C=O). HR-MS: 551.2056 ($[M+H]^+$, $C_{29}H_{32}ClN_4O_5^+$; calc. 551.2061).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(2-Chlorophenyl)amino]carbonyl}hydrazide (**6k**). Recrystallization from EtOH. Yield 0.474 g (86%). M.p. 167–168°. IR: 3487*w*, 3279*w*, 3043*w*, 2960*m*, 1694*s*, 1667*s*, 1616*m*, 1596*m*. ^{1}H-NMR: 9.80 (*s*, NH); 8.91 (*s*, NH); 8.12 (br., NH); 8.10 (*d*, *J*(3′,4′) = 7.8, H–C(3′)); 7.50 (*d*, *J*(6′,5′) = 8.1, H–C(6′)); 7.08–7.33 (*m*, H–C(4′), H–C(5′)); 6.68 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.57 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.69 (*d*, *J*(18,19) = 8.8, H–C(18)); 5.50 (*d*, *J*(18,19) = 8.8, H–C(19)); 4.62 (*s*, H_β–C(5)); 3.76 (*s*, MeO–C(3)); 3.52 (*s*, MeO–C(6)); 3.22 (*d*, *J*(9α,10α) = 6.4, H_α–C(9)); 3.17 (*d*, *J*(10α,10β) = 18.4, H_β–C(10)); 2.56–2.96 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.47 (*dd*, *J*(10α,10β) = 18.5, *J*(9α,10α) = 6.3, H_α–C(10)); 2.36 (*s*, MeN); 1.73–2.31 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.27 (*dd*, *J*(8α,8β) = 12.1, *J*(7β,8α) = 6.2, H_α–C(8)). ^{13}C-NMR: 22.2 (C(10)); 31.5 (C(8)); 33.5 (C(15)); 41.2 (C(7)); 43.0 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.1 (C(13)); 59.6 (C(9)); 52.3 (*Me*O–C(6)); 56.5 (*Me*O–C(3)); 80.1 (C(6)); 93.0 (C(5)); 113.8 (C(2)); 114.3 (C(6′)); 119.8 (C(1)); 121.1 (C(3′)); 123.9 (C(5′)); 127.1 (C(18)); 128.8 (C(12)); 134.3 (C(11)); 128.1 (C(4′)); 129.7 (C(2′)); 135.1 (C(19)); 136.2 (C(1′)); 141.6 (C(3)); 148.1 (C(4)); 155.24 (C=O); 171.9 (C=O). HR-MS: 551.2064 ($[M+H]^+$, $C_{29}H_{32}ClN_4O_5^+$; calc. 551.2061).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(4-Bromophenyl)amino]carbonyl}hydrazide (**6l**). Recrystallization from EtOH/$CHCl_3$. Yield 0.422 g (71%). M.p. 154–155°. IR: 3346*w*, 3252*w*, 3063*w*, 2963*m*, 1703*s*, 1662*s*, 1627*m*, 1598*m*. ^{1}H-NMR: 9.70 (*s*, NH); 8.51 (br., NH); 8.29 (*s*, NH); 7.44 (*d*, *J*(2′,3′) = 9.0, H–C(2′,6′)); 7.40 (*d*, *J*(2′,3′) = 9.0, H–C(3′,5′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.52 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.59 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.46 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.61 (*s*, H_β–C(5)); 3.71 (*s*, MeO–C(3)); 3.51 (*s*, MeO–C(6)); 3.18 (*d*, *J*(9α,10α) = 6.2, H_α–C(9)); 3.12 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.49–2.88 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.42 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.2, H_α–C(10)); 2.30 (*s*, MeN); 1.75–2.24 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.32 (*dd*, *J*(8α,8β) = 11.7, *J*(7β,8α) = 5.8, H_α–C(8)). ^{13}C-NMR: 22.2 (C(10)); 30.8 (C(8)); 33.5 (C(15)); 40.9 (C(7)); 43.0 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.3 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.5 (C(9)); 81.3 (C(6)); 92.6 (C(5)); 113.7 (C(2)); 113.9 (C(4′)); 119.8 (C(1)); 120.7 (C(2′)); 127.1 (C(18)); 128.8 (C(12)); 132.0 (C(3′)); 134.3 (C(11)); 135.3 (C(19)); 141.6 (C(3)); 139.4 (C(1′)); 148.0 (C(4)); 155.6 (C=O); 172.0 (C=O). HR-MS: 595.1546 ($[M+H]^+$, $C_{29}H_{32}BrN_4O_5^+$; calc. 595.1556).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(3-Bromophenyl)amino]carbonyl}hydrazide (**6m**). Recrystallization from EtOH. Yield 0.446 g (75%). M.p. 178–179°. IR: 3501*w*, 3462*w*, 3285*w*, 3066*w*, 2980*m*, 1701*s*, 1668*s*, 1618*m*, 1608*m*. ^{1}H-NMR: 9.67 (*s*, NH); 8.62 (br., NH); 7.96 (*s*, NH); 7.83 (*s*, H–C(2′)); 7.21–7.29 (*m*, H–C(4′), H–C(5′)); 7.14 (*d*, *J*(5′,6′) = 7.8, H–C(6′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.52 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.60 (*d*, *J*(18,19) = 8.8, H–C(18)); 5.45 (*d*, *J*(18,19) = 8.8, H–C(19)); 4.60 (*s*, H_β–C(5)); 3.71 (*s*, MeO–C(3)); 3.51 (*s*, MeO–C(6)); 3.18 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.13 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.90–2.51 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.42 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.4, H_α–C(10)); 2.31 (*s*, MeN); 2.26 (*m*, H_{ax}–C(16)); 1.93 (*m*, H_{ax}–C(15)); 1.75 (*m*, H_{eq}–C(15)); 1.30 (*dd*, *J*(8α,8β) = 11.9, *J*(7β,8α) = 5.8, H_α–C(8)). ^{13}C-NMR: 22.2 (C(10)); 31.1 (C(8)); 33.5 (C(15)); 41.0 (C(7)); 43.0 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.3 (*Me*O–C(6)); 56.5 (*Me*O–C(3)); 59.5 (C(9)); 81.2 (C(6)); 92.8 (C(5)); 113.8 (C(2)); 117.6 (C(6′)); 119.8 (C(1)); 121.0 (C(5′)); 122.1 (C(3′)); 125.0 (C(4′)); 127.1 (C(18)); 128.8 (C(12)); 131.2 (C(2′)); 134.3 (C(11)); 135.3 (C(19)); 141.6 (C(3)); 141.7 (C(1′)); 148.0 (C(4)); 155.5 (C=O); 172.0 (C=O). HR-MS: 595.1543 ($[M+H]^+$, $C_{29}H_{32}BrN_4O_5^+$; calc. 595.1556).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(2-Bromophenyl)amino]carbonyl}hydrazide (**6n**). Recrystallization from $CHCl_3$/hexane. Yield 0.494 g (83%). M.p. 156–157°. IR: 3315*w*, 3285*w*, 3066*w*, 2980*m*, 1702*s*, 1667*s*, 1627*m*, 1614*m*. ^{1}H-NMR: 9.80 (*s*, NH); 8.99 (br., NH); 7.98 (*s*, NH); 8.03 (*d*, *J*(3′,4′) = 7.8, H–C(3′)); 7.65 (*d*, *J*(6′,5′) = 8.0, H–C(6′)); 7.02–7.39 (*m*, H–C(4′), H–C(5′)); 6.68 (*d*, *J*(1,2) = 8.0, H–C(2)); 6.57 (*d*, *J*(1,2) = 8.0, H–C(1)); 5.71 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.50 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.61 (*s*, H_β–C(5)); 3.76 (*s*, MeO–C(3)); 3.52 (*s*, MeO–C(6)); 3.20 (*d*, *J*(9α,10α) = 6.2, H_α–C(9)); 3.17 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.55–

2.96 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.48 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.3, H_α–C(10)); 2.36 (*s*, MeN); 1.81–2.30 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.32 (*dd*, *J*(8α,8β) = 12.0, *J*(7β,8α) = 6.2, H_α–C(8)). ^{13}C-NMR: 21.7 (C(10)); 31.0 (C(8)); 33.0 (C(15)); 40.7 (C(7)); 43.1 (C(14)); 43.6 (MeN); 45.0 (C(16)); 46.5 (C(13)); 52.3 (*Me*O–C(6)); 56.5 (*Me*O–C(3)); 59.0 (C(9)); 80.4 (C(6)); 92.60 (C(5)); 113.3 (C(2)); 115.1 (C(5′)); 119.3 (C(1)); 124.1 (C(6′)); 125.8 (C(2′)); 126.7 (C(18)); 128.1 (C(4′)); 128.3 (C(12)); 132.4 (C(3′)); 133.8 (C(11)); 134.6 (C(19)); 136.8 (C(1′)); 141.1 (C(3)); 147.6 (C(4)); 154.8 (C=O); 171.4 (C=O). HR-MS: 595.1551 ($[M+H]^+$, $C_{29}H_{32}BrN_4O_5^+$; calc. 595.1556).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(4-Iodophenyl)amino]carbonyl}hydrazide (**6o**). Recrystallization from EtOH/$CHCl_3$. Yield 0.463 g (72%). M.p. 168–169°. IR: 3514*w*, 3272*w*, 3066*w*, 2960*m*, 1693*s*, 1665*m*, 1641*m*, 1641*m*. ^{1}H-NMR: 9.69 (*s*, NH); 8.50 (br., NH); 8.27 (*s*, NH); 7.59 (*d*, *J*(2′,3′) = 8.7, H–C(2′,6′)); 7.27 (*d*, *J*(2′,3′) = 8.7, H–C(3′,5′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.52 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.58 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.45 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.60 (*s*, H_β–C(5)); 3.71 (*s*, MeO–C(3)); 3.50 (*s*, MeO–C(6)); 3.18 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.12 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.50–2.87 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.42 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.4, H_α–C(10)); 2.30 (*s*, MeN); 1.75–2.24 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.30 (*dd*, *J*(8α,8β) = 11.7, *J*(7β,8α) = 5.7, H_α–C(8)). ^{13}C-NMR: 22.2 (C(10)); 30.8 (C(8)); 33.5 (C(15)); 40.9 (C(7)); 43.0 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.3 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.5 (C(9)); 81.2 (C(6)); 85.4 (C(4′)); 92.6 (C(5)); 113.7 (C(2)); 119.8 (C(1)); 121.1 (C(2′)); 127.1 (C(18)); 128.8 (C(12)); 134.3 (C(11)); 135.3 (C(19)); 137.8 (C(3′)); 139.8 (C(1′)); 141.6 (C(3)); 148.0 (C(4)); 155.6 (C=O); 172.0 (C=O). HR-MS: 643.1439 ($[M+H]^+$, $C_{29}H_{32}IN_4O_5^+$; calc. 643.1417).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(3-Iodophenyl)amino]carbonyl}hydrazide (**6p**). Recrystallization from EtOH. Yield 0.502 g (78%). M.p. 134–135°. IR: 3443*w*, 3267*w*, 3065*w*, 2971*w*, 1691*s*, 1678*s*, 1612*m*, 1602*m*. ^{1}H-NMR: 9.66 (*s*, NH); 8.52 (br., NH); 8.29 (*s*, NH); 7.96 (*s*, H–C(2′)); 7.04–7.32 (*m*, H–C(4′), H–C(5′), H–C(6′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.52 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.60 (*d*, *J*(18,19) = 8.8, H–C(18)); 5.45 (*d*, *J*(18,19) = 8.8, H–C(19)); 4.60 (*s*, H_β–C(5)); 3.71 (*s*, MeO–C(3)); 3.50 (*s*, MeO–C(6)); 3.18 (*m*, H_α–C(9)); 3.08 (*d*, *J*(10α,10β) = 18.9, H_β–C(10)); 2.51–2.90 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.44 (*m*, H_α–C(10)); 2.31 (*s*, MeN); 1.75–2.29 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.30 (*dd*, *J*(8α,8β) = 11.6, *J*(7β,8α) = 5.9, H_α–C(8)). ^{13}C-NMR: 22.3 (C(10)); 31.2 (C(8)); 33.5 (C(15)); 41.0 (C(7)); 43.0 (C(14)); 43.5 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.3 (*Me*O–C(6)); 56.5 (*Me*O–C(3)); 59.6 (C(9)); 81.2 (C(6)); 92.7 (C(5)); 95.2 (C(3′)); 113.8 (C(2)); 118.1 (C(6′)); 119.8 (C(1)); 126.9 (C(4′)); 127.2 (C(18)); 128.7 (C(12)); 130.9 (C(5′)); 131.2 (C(2′)); 134.3 (C(11)); 135.2 (C(19)); 141.6 (C(3)); 141.7 (C(1′)); 148.0 (C(4)); 155.5 (C=O); 172.0 (C=O). HR-MS: 643.1415 ($[M+H]^+$, $C_{29}H_{32}IN_4O_5^+$; calc. 643.1417).

(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxylic Acid 2-{[(2-Iodophenyl)amino]carbonyl}hydrazide (**6q**). Recrystallization from DMSO/H_2O. Yield 0.457 g (71%). M.p. 159–160°. IR: 3514*w*, 3279*w*, 3056*w*, 2977*m*, 1694*s*, 1667*s*, 1616*m*, 1596*m*. ^{1}H-NMR: 9.80 (*s*, NH); 8.95 (br., NH); 7.75 (*s*, NH); 7.87 (*d*, *J*(3′,4′) = 8.0, H–C(3′)); 7.83 (*d*, *J*(6′,5′) = 8.0, H–C(6′)); 6.78–7.39 (*m*, H–C(4′), H–C(5′)); 6.67 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.57 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.70 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.51 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.61 (*s*, H_β–C(5)); 3.76 (*s*, MeO–C(3)); 3.52 (*s*, MeO–C(6)); 3.22 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.17 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.55–2.96 (*m*, H_β–C(8), H_β–C(7), H_{eq}–C(16)); 2.47 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.3, H_α–C(10)); 2.33 (*s*, MeN); 1.80–2.30 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.32 (*dd*, *J*(8α,8β) = 12.0, *J*(7β,8α) = 6.2, H_α–C(8)). ^{13}C-NMR: 22.2 (C(10)); 31.4 (C(8)); 33.5 (C(15)); 41.2 (C(7)); 43.0 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.1 (C(13)); 52.4 (*Me*O–C(6)); 56.5 (*Me*O–C(3)); 59.6 (C(9)); 80.9 (C(6)); 93.1 (C(5)); 113.8 (C(2)); 119.8 (C(1)); 122.9 (C6′)); 124.0 (C5′)); 127.1 (C(18)); 128.8 (C(12)); 129.1 (C4′)); 134.3 (C(11)); 135.1 (C(19)); 139.4 (C3′)); 140.1 (C(2′)); 140.4 (C(1′)); 141.6 (C(3)); 148.1 (C(4)); 155.4 (C=O)); 171.9 (C=O). HR-MS: 643.1423 ($[M+H]^+$, $C_{29}H_{32}IN_4O_5^+$; calc. 643.1417).

Compounds **7a**–**7q**: *General Procedure.* A mixture of the corresponding hydrazide **6a**–**6q** (0.5 mmol) and $POCl_3$ (12 ml) was heated at 90° under stirring for 3 h (TLC control). Then, the mixture was allowed to cool to r.t. After stirring for an additional 30 min, the resulting soln. was poured into ice-cold H_2O and made alkaline to pH 8 with a NaOH soln. The precipitated product was filtered, purified by CC, and recrystallized from an appropriate solvent.

N-*{5-[(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}benzenamine* (**7a**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from EtOH. Yield 0.167 g (67%). M.p. 176–177°. IR: 3357*w*, 3057*w*, 2961*m*. ^{1}H-NMR[1]): 10.52 (*s*, NH); 7.49 (*d*, *J*(2′,3′) = 7.8, H–C(2′,6′)); 7.14–7.39 (*m*, H–C(3′), H–C(5′), H–C(4′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.55 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.61 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.52 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.76 (*s*, H_β–C(5)); 3.74 (*m*, H_β–C(7)); 3.72 (*s*, MeO–C(3)); 3.61 (*s*, MeO–C(6)); 3.21 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.14 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.51–3.10 (*m*, H_β–C(8), H_{eq}–C(16)); 2.45 (*dd*, *J*(10α,10β) = 18.6, *J*(9α,10α) = 6.3, H_α–C(10)); 2.32 (*s*, MeN); 1.79–2.27 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.35 (*dd*, *J*(8α,8β) = 12.3, *J*(7β,8α) = 5.9, H_α–C(8)). ^{13}C-NMR[1]): 22.2 (C(10)); 33.0 (C(15)); 31.4 (C(8)); 33.6 (C(7)); 42.9 (C(14)); 45.6 (C(16)); 47.0 (C(13)); 59.6 (C(9)); 81.0 (C(6)); 90.9 (C(5)); 113.7 (C(2)); 118.1 (C(4′)); 119.9 (C(1)); 120.2 (C(2′)); 127.6 (C(18)); 128.6 (C(12)); 131.1 (C(3′)); 134.4 (C(11)); 137.0 (C(19)); 138.2 (C(1′)); 141.6 (C(3)); 147.8 (C(4)); 160.2 (C=N); 160.6 (C=N). HR-MS: 499.2355 ([*M* + H]$^+$, $C_{29}H_{31}N_4O_4^+$; calc. 499.2345).

N-*{5-[(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-4-methylbenzenamine* (**7b**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from MeOH. Yield 0.151 g (59%). M.p. 142–143°. IR: 3257*w*, 3036*w*, 2925*m*. ^{1}H-NMR[1]): 10.25 (*s*, NH); 7.42 (*d*, *J*(2′,3′) = 8.5, H–C(2′,6′)); 7.11 (*d*, *J*(2′,3′) = 8.5, H–C(3′,5′)); 6.64 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.54 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.63 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.57 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.90 (*s*, H_β–C(5)); 3.75 (*m*, H_β–C(7)); 3.70 (*s*, MeO–C(3)); 3.43 (*s*, MeO–C(6)); 3.20 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.14 (*d*, *J*(10α,10β) = 19.0, H_β–C(10)); 2.45–3.07 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10)); 2.30 (*s*, MeN); 2.18 (*s*, Me–C(4′)); 1.70–2.25 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.47 (*dd*, *J*(8α,8β) = 12.8, *J*(7β,8α) = 6.3, H_α–C(8)). ^{13}C-NMR[1]): 20.8 (*Me*–C(4′)); 22.2 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.7 (C(7)); 42.9 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.4 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 81.0 (C(6)); 90.9 (C(5)); 113.7 (C(2)); 117.2 (C(3′)); 119.9 (C(1)); 127.6 (C(18)); 128.6 (C(12)); 129.8 (C(2′)); 130.8 (C(4′)); 134.4 (C(11)); 136.9 (C(1′)); 137.0 (C(19)); 141.7 (C(3)); 147.8 (C(4)); 160.3 (C=N); 160.4 (C=N). HR-MS: 513.2371 ([*M* + H]$^+$, $C_{30}H_{33}N_4O_4^+$; calc. 513.2502).

N-*{5-[(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-2-methylbenzenamine* (**7c**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from $CHCl_3$/hexane. Yield 0.172 g (67%). M.p. 117–118°. IR: 3219*w*, 3031*w*, 2930*m*. ^{1}H-NMR[1]): 9.32 (*s*, NH); 7.62 (*d*, *J*(3′,4′) = 7.8, H–C(3′)); 6.97–7.24 (*m*, H–C(4′), H–C(5′), H–C(6′)); 6.64 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.54 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.62 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.57 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.88 (*s*, H_β–C(5)); 3.71 (*s*, MeO–C(3)); 3.68 (*m*, H_β–C(7)); 3.41 (*s*, MeO–C(6)); 3.20 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.13 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 3.07 (*dd*, *J*(8α,8β) = 12.6, *J*(7β,8β) = 9.8, H_β–C(8); 2.25–2.50 (*m*, H_{eq}–C(16), H_α–C(10), H_{ax}–C(16)); 2.30 (*s*, MeN); 2.24 (*s*, Me–C(2′)); 1.70–2.12 (*m*, H_{ax}–C(15), H_{eq}–C(15)); 1.50 (*dd*, *J*(8α,8β) = 12.6, *J*(7β,8α) = 6.2, H_α–C(8)). ^{13}C-NMR[1]): 20.8 (*Me*–C(2′)); 22.2 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.7 (C(7)); 42.9 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.4 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 81.0 (C(6)); 90.9 (C(5)); 113.7 (C(2)); 117.2 (C(3′)); 119.9 (C(1)); 127.6 (C(18)); 128.6 (C(12)); 129.8 (C(2′)); 130.8 (C(4′)); 134.4 (C(11)); 136.9 (C(1′)); 137.0 (C(19)); 141.7 (C(3)); 147.8 (C(4)); 160.3 (C=N); 160.4 (C=N). HR-MS: 513.2417 ([*M* + H]$^+$, $C_{30}H_{33}N_4O_4^+$; calc. 513.2502).

N-*{5-[(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-4-methoxybenzenamine* (**7d**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from AcOEt/hexane. Yield 0.135 g (51%). M.p. 136–138°. IR: 3242*w*, 3037*w*, 2931*w*. ^{1}H-NMR[1]): 10.06 (*s*, NH); 7.39 (*d*, *J*(2′,3′) = 9.0, H–C(2′,6′)); 6.84 (*d*, *J*(2′,3′) = 8.7, H–C(3′,5′)); 6.57 (*d*, *J*(1,2) = 8.2, H–C(1)); 6.47 (*d*, *J*(1,2) = 8.2, H–C(2)); 5.55 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.49 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.90 (*s*, H_β–C(5)); 3.68 (*m*, H_β–C(7)); 3.64 (*s*, MeO–C(3)); 3.63 (*s*, MeO–C(4′)); 3.35 (*s*, MeO–C(6)); 3.13 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.06 (*d*, *J*(10α,10β) = 18.8, H_β–C(10)); 3.00 (*dd*, *J*(8α,8β) = 12.6, *J*(7β,8β) = 9.8, H_β–C(8)); 2.23 (*s*, MeN); 1.63–2.44 (*m*, H_{eq}–C(16), H_α–C(10), H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.47 (*dd*, *J*(8α,8β) = 12.6, *J*(7β,8α) = 6.2, H_α–C(8)). ^{13}C-NMR[1]):

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[1]) For convenience, the unprimed locants are retained for the morphinan moiety of **7a**–**7q** (see *Scheme*).

22.2 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.7 (C(7)); 42.9 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.4 (*Me*O–C(6)); 55.6 (*Me*O–C(4′)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 81.0 (C(6)); 90.9 (C(5)); 113.7 (C(2)); 113.7 (C(3′)); 118.6 (C(2′)); 119.9 (C(1)); 128.6 (C(12)); 127.6 (C(18)); 132.6 (C(1′)); 134.4 (C(11)); 137.0 (C(19)); 141.7 (C(3)); 147.8 (C(4)); 154.6 (C(4′)); 160.3 (C=N); 160.4 (C=N). HR-MS: 529.2433 ($[M+H]^+$, $C_{30}H_{33}N_4O_5^+$; calc. 529.2451).

N-*{5-[(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-3-methoxybenzenamine* (**7e**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from MeOH. Yield 0.148 g (56%). M.p. 89–90°. IR: 3258*w*, 3061*w*, 2932*m*. ^{1}H-NMR[1]): 10.37 (*s*, NH); 7.04–7.23 (*m*, H–C(2′), H–C(4′), H–C(5′), H–C(6′)); 6.64 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.55 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.63 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.57 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.90 (*s*, H_β–C(5)); 3.76 (*m*, H_β–C(7)); 3.73 (*s*, MeO–C(3′)); 3.70 (*s*, MeO–C(3)); 3.41 (*s*, MeO–C(6)); 3.21 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.14 (*d*, *J*(10α,10β) = 19.2, H_β–C(10)); 3.08 (*dd*, *J*(8α,8β) = 13.0, *J*(7β,8β) = 9.8, H_β–C(8)); 2.20 (*s*, MeN); 1.71–2.49 (*m*, H_{eq}–C(16), H_α–C(10), H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.49 (*dd*, *J*(8α,8β) = 13.0, *J*(7β,8α) = 6.4, H_α–C(8)). ^{13}C-NMR[1]): 22.1 (C(10)); 31.4 (C(8)); 33.0 (C(15)); 33.7 (C(7)); 42.9 (C(14)); 43.5 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.4 (*Me*O–C(6)); 55.4 (*Me*O–C(3′)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 80.9 (C(6)); 91.0 (C(5)); 111.1 (C(2′)); 113.8 (C(2)); 116.5 (C(6′)); 119.5 (C(4′)); 119.9 (C(1)); 127.5 (C(19)); 128.6 (C(12)); 130.9 (C(5′)); 134.3 (C(11)); 137.1 (C(18)); 140.6 (C(1′)); 141.7 (C(3)); 147.8 (C(4)); 151.4 (C(3′)); 160.1 (C=N); 162.6 (C=N). HR-MS: 529.2433 ($[M+H]^+$, $C_{30}H_{33}N_4O_5^+$; calc. 529.2451).

N-*{5-[(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-2-methoxybenzenamine* (**7f**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from AcOEt/hexane. Yield 0.140 g (53%). M.p. 85–86°. IR: 3258*w*, 3052*w*, 2936*m*. ^{1}H-NMR[1]): 9.36 (*s*, NH); 6.93–7.92 (*m*, H–C(3′), H–C(4′), H–C(5′), H–C(6′)); 6.64 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.53 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.62 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.55 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.88 (*s*, H_β–C(5)); 3.85 (*s*, MeO–C(2′)); 3.71 (*s*, MeO–C(3)); 3.68 (*m*, H_β–C(7)); 3.42 (*s*, MeO–C(6)); 3.20 (*d*, *J*(9α,10α) = 6.3, H_α–C(9)); 3.13 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 3.06 (*dd*, *J*(8α,8β) = 12.5, *J*(7β,8β) = 9.7, H_β–C(8)); 2.30 (*s*, MeN); 1.70–2.49 (*m*, H_{eq}–C(16), H_α–C(10), H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.50 (*dd*, *J*(8α,8β) = 12.5, *J*(7β,8α) = 6.2, H_α–C(8)). ^{13}C-NMR[1]): 22.2 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.8 (C(7)); 42.9 (C(14)); 43.6 (MeN); 45.5 (C(16)); 46.9 (C(13)); 55.4 (*Me*O–C(3)); 56.1 (*Me*O–C(2′)); 56.4 (*Me*O–C(6)); 59.6 (C(9)); 81.1 (C(6)); 91.0 (C(5)); 111.6 (C(3′)); 113.8 (C(2)); 118.9 (C(6′)); 119.9 (C(1)); 121.0 (C(4′)); 123.3 (C(5′); 127.5 (C(18)); 128.1 (C(1′)); 128.6 (C(12)); 134.5 (C(11)); 136.9 (C(19)); 141.7 (C(3)); 147.8 (C(4)); 149.0 (C(2′)); 160.8 (C=N); 161.0 (C=N). HR-MS: 529.2452 ($[M+H]^+$, $C_{30}H_{33}N_4O_5^+$; calc. 529.2451).

4-Fluoro-N-*{5-[(5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-benzenamine* (**7g**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from AcOEt/hexane. Yield 0.145 g (56%). M.p. 182–183°. IR: 3204*w*, 3061*w*, 2928*w*. ^{1}H-NMR[1]): 10.51 (*s*, NH); 7.08–7.57 (*m*, H–C(2′,6′), H–C(3′,5′)); 6.64 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.54 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.63 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.57 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.89 (*s*, H_β–C(5)); 3.75 (*dd*, *J*(7β,8β) = 8.9, *J*(7β,8α) = 6.2, H_β–C(7)); 3.71 (*s*, MeO–C(3)); 3.42 (*s*, MeO–C(6)); 3.20 (*d*, *J*(9α,10α) = 6.1, H_α–C(9)); 3.14 (*d*, *J*(10α,10β) = 18.9, H_β–C(10)); 2.30 (*s*, MeN); 1.70–3.07 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10), H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.50 (*dd*, *J*(8α,8β) = 12.6, *J*(7β,8α) = 6.2, H_α–C(8)). ^{13}C-NMR[1]): 22.2 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.7 (C(7)); 42.9 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.4 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 80.9 (C(6)); 90.9 (C(5)); 113.7 (C(2)); 115.9–116.1 (*J*(C(3′),F) = 22.3, C(3′)); 118.8 (*J*(C(2′),F) = 7.9, C(2′)); 119.9 (C(1)); 127.5 (C(18)); 128.6 (C(12)); 134.4 (C(11)); 135.8 (C(1′)); 137.1 (C(19)); 141.7 (C(3)); 147.8 (C(4)); 156.3–158.7 (*J*(C(4′),F) = 236.9, C(4′)); 160.3 (C=N); 160.4 (C=N). HR-MS: 517.2213 ($[M+H]^+$, $C_{29}H_{30}FN_4O_4^+$; calc. 517.2251).

2-Fluoro-N-*{5-[(5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-benzenamine* (**7h**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from AcOEt/hexane. Yield 0.165 g (64%). M.p. 117–118°. IR: 3232*w*, 3071*w*, 2924*m*. ^{1}H-NMR[1]): 10.48 (*s*, NH); 7.14–7.64 (*m*, H–C(3′), H–C(4′), H–C(5′), H–C(6′)); 6.64 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.54 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.64 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.57 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.89 (*s*, H_β–C(5)); 3.75 (*m*, H_β –C(7)); 3.71 (*s*, MeO–C(3)); 3.41 (*s*, MeO–C(6)); 3.18 (*d*, *J*(9α,10α) = 6.2,

H_α–C(9)); 3.14 (*d*, *J*(10*α*,10*β*) = 18.8, H_β–C(10)); 2.30 (*s*, MeN); 1.69–3.07 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10), H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.50 (*dd*, *J*(8*α*,8*β*) = 12.5, *J*(7*β*,8*α*) = 6.3, H_α–C(8)). ^{13}C-NMR[1]): 22.2 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.6 (C(7)); 42.9 (C(14)); 43.5 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.4 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 81.0 (C(6)); 90.9 (C(5)); 113.7 (C(2)); 114.3–115.9 (*J*(C(3′),F) = 22.7, C(3′)); 119.2 (*J*(C(4′),F) = 7.7, C(4′)); 119.9 (C(1)); 127.5 (C(18)); 128.6 (C(12)); 134.4 (C(11)); 135.8–135.9 (*J*(C(1′),F) = 9.8, C(1′)); 137.0 (C(19)); 141.7 (C(3)); 147.7 (C(4)); 152.5–154.7 (*J*(C(2′),F) = 234.8, C(2′)); 160.3 (C=N); 161.2 (C=N). HR-MS: 517.2226 ([*M* + H]$^+$, $C_{29}H_{30}FN_4O_4^+$; calc. 517.2251).

4-Chloro-N-*{5-[(5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-benzenamine* (**7i**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from AcOEt/hexane. Yield 0.163 g (61%). M.p. 132–133°. IR: 3258*w*, 3055*w*, 2929*w*. ^{1}H-NMR[1]): 9.56 (*s*, NH); 7.56 (*d*, *J*(2′,3′) = 8.9, H–C(3′,5′)); 7.37 (*d*, *J*(2′,3′) = 8.9, H–C(2′,6′)); 6.64 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.54 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.64 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.58 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.90 (*s*, H_β–C(5)); 3.70 (*s*, MeO–C(3)); 3.43 (*s*, MeO–C(6)); 3.76 (*dd*, *J*(7*β*,8*β*) = 9.4, *J*(7*β*,8*α*) = 6.5, H_β–C(7)); 3.20 (*d*, *J*(9*α*,10*α*) = 6.1, H_α–C(9)); 3.14 (*d*, *J*(10*α*,10*β*) = 19.0, H_β–C(10)); 2.30 (*s*, MeN); 3.06–1.70 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10), H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.47 (*dd*, *J*(8*α*,8*β*) = 12.8, *J*(7*β*,8*α*) = 6.4, H_α–C(8)). ^{13}C-NMR[1]): 21.7 (C(10)); 30.9 (C(15)); 32.5 (C(8)); 33.3 (C(7)); 42.4 (C(14)); 43.1 (MeN); 45.0 (C(16)); 46.5 (C(13)); 50.9 (*Me*O–C(6)); 55.9 (*Me*O–C(3)); 59.1 (C(9)); 80.5 (C(6)); 90.4 (C(5)); 113.3 (C(2)); 118.3 (C(3′)); 119.4 (C(1)); 125.1 (C(4′)); 127.1 (C(18)); 128.1 (C(12)); 128.8 (C(2′)); 133.9 (C(11)); 136.6 (C(19)); 137.8 (C(1′)); 141.2 (C(3)); 147.3 (C(4)); 159.6 (C=N); 160.1 (C=N). HR-MS: 533.1948 ([*M* + H]$^+$, $C_{29}H_{30}ClN_4O_4^+$; calc. 533.1956).

3-Chloro-N-*{5-[(5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-benzenamine* (**7j**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from AcOEt/hexane. Yield 0.173 g (65%). M.p. 236–237°. IR: 3331*w*, 3065*w*, 2929*m*. ^{1}H-NMR[1]): 10.70 (*s*, NH); 7.70 (*s*, H–C(2′)); 7.00–7.37 (*m*, H–C(4′), H–C(5′), H–C(6′)); 6.64 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.54 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.64 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.58 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.90 (*s*, H_β–C(5)); 3.78 (*m*, H_β–C(7)); 3.71 (*s*, MeO–C(3)); 3.43 (*s*, MeO–C(6)); 3.21 (*d*, *J*(9*α*,10*α*) = 6.3, H_α–C(9)); 3.14 (*d*, *J*(10*α*,10*β*) = 19.3, H_β–C(10)); 2.44–3.08 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10)); 2.31 (*s*, MeN); 1.72–2.25 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.47 (*dd*, *J*(8*α*,8*β*) = 12.7, *J*(7*β*,8*α*) = 6.1, H_α–C(8)). ^{13}C-NMR[1]): 22.2 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.8 (C(7)); 42.9 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.4 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 81.0 (C(6)); 90.9 (C(5)); 113.7 (C(2)); 115.9 (C(6′)); 116.6 (C(2′)); 119.9 (C(1)); 121.1 (C(4′)); 127.6 (C(18)); 128.6 (C(12)); 131.1 (C(5′)); 133.9 (C(3′)); 134.4 (C(11)); 137.1 (C(19)); 140.8 (C(1′)); 141.7 (C(3)); 147.8 (C(4)); 160.0 (C=N); 160.7 (C=N). HR-MS: 533.1964 ([*M* + H]$^+$, $C_{29}H_{30}ClN_4O_4^+$; calc. 533.1956).

2-Chloro-N-*{5-[(5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-benzenamine* (**7k**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from AcOEt/hexane. Yield 0.187 g (70%). M.p. 161–162°. IR: 3331*w*, 3065*w*, 2929*m*. ^{1}H-NMR[1]): 9.72 (*s*, NH); 7.04–7.90 (*m*, H–C(3′), H–C(4′), H–C(5′), H–C(6′)); 6.64 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.54 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.64 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.58 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.90 (*s*, H_β–C(5)); 3.73 (*m*, H_β –C(7)); 3.71 (*s*, MeO–C(3)); 3.43 (*s*, MeO–C(6)); 3.21 (*d*, *J*(9*α*,10*α*) = 6.3, H_α–C(9)); 3.14 (*d*, *J*(10*α*,10*β*) = 19.2, H_β–C(10)); 2.44–3.08 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10)); 2.31 (*s*, MeN); 1.72–2.25 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.47 (*dd*, *J*(8*α*,8*β*) = 12.8, *J*(7*β*,8*α*) = 6.4, H_α–C(8)). ^{13}C-NMR[1]): 22.2 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.8 (C(7)); 42.9 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.5 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 81.0 (C(6)); 91.0 (C(5)); 113.8 (C(2)); 119.9 (C(1)); 122.2 (C(2′)); 124.1 (C(3′)); 124.9 (C(4′)); 127.4 (C(18)); 128.3 (C(6′)); 128.6 (C(12)); 130.2 (C(5′)); 134.4 (C(11)); 136.0 (C(1′)); 137.0 (C(19)); 141.7 (C(3)); 147.8 (C(4)); 160.9 (C=N); 161.4 (C=N). HR-MS: 533.1964 ([*M* + H]$^+$, $C_{29}H_{30}ClN_4O_4^+$; calc. 533.1956).

4-Bromo-N-*{5-[(5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-benzenamine* (**7l**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from AcOEt/hexane. Yield 0.205 g (71%). M.p. 144–145°. IR: 3251*w*, 3031*w*, 2929*w*. ^{1}H-NMR[1]): 10.58 (*s*, NH); 7.51 (*s*, H–C(2′,6′), H–C(3′,5′)); 6.64 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.54 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.64 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.57 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.90 (*s*, H_β–C(5)); 3.70 (*s*, MeO–C(3)); 3.42 (*s*, MeO–C(6)); 3.77 (*m*, H_β–C(7)); 3.20 (*d*, *J*(9*α*,10*α*) = 6.0, H_α–C(9)); 3.14 (*d*,

$J(10\alpha,10\beta) = 19.0$, H_β–C(10)); 2.46–3.06 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10)); 2.30 (*s*, MeN); 1.70–2.25 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.47 (*dd*, $J(8\alpha,8\beta) = 12.7$, $J(7\beta,8\alpha) = 6.2$, H_α–C(8)). ^{13}C-NMR[1]): 22.1 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.8 (C(7)); 42.9 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.4 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 81.0 (C(6)); 90.9 (C(5)); 113.5 (C(4′)); 113.7 (C(2)); 119.3 (C(3′)); 119.9 (C(1)); 127.6 (C(18)); 128.6 (C(12)); 132.2 (C(2′)); 134.4 (C(11)); 137.1 (C(19)); 138.7 (C(1′)); 141.7 (C(3)); 147.8 (C(4)); 160.1 (C=N); 160.6 (C=N). HR-MS: 577.1465 ($[M+H]^+$, $C_{29}H_{30}BrN_4O_4^+$; calc. 577.1450).

3-Bromo-N-*{5-[(5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-benzenamine* (**7m**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from AcOEt/hexane. Yield 0.190 g (66%). M.p. 215–216°. IR: 3259*w*, 3053*w*, 2937*m*. ^{1}H-NMR[1]): 10.56 (*s*, NH); 7.76 (*s*, H–C(2′)); 7.05–7.38 (*m*, H–C(4′), H–C(5′), H–C(6′)); 6.64 (*d*, $J(1,2) = 8.2$, H–C(2)); 6.55 (*d*, $J(1,2) = 8.2$, H–C(1)); 5.54 (*d*, $J(18,19) = 8.7$, H–C(18)); 5.49 (*d*, $J(18,19) = 8.7$, H–C(19)); 4.81 (*s*, H_β–C(5)); 3.69 (*m*, H_β–C(7)); 3.61 (*s*, MeO–C(3)); 3.34 (*s*, MeO–C(6)); 3.12 (*d*, $J(9\alpha,10\alpha) = 6.2$, H_α–C(9)); 3.01 (*d*, $J(10\alpha,10\beta) = 19.1$, H_β–C(10)); 2.35–2.99 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10)); 2.21 (*s*, MeN); 1.62–2.18 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.39 (*dd*, $J(8\alpha,8\beta) = 12.8$, $J(7\beta,8\alpha) = 6.3$, H_α–C(8)). ^{13}C-NMR[1]): 22.1 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.8 (C(7)); 42.9 (C(14)); 43.5 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.4 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 80.9 (C(6)); 90.9 (C(5)); 113.8 (C(2)); 116.3 (C(6′)); 119.5 (C(2′)); 119.9 (C(1)); 122.4 (C(3′)); 124.6 (C(4′)); 127.5 (C(18)); 128.6 (C(12)); 131.4 (C(5′)); 134.4 (C(11)); 137.1 (C(19)); 140.9 (C(1′)); 141.7 (C(3)); 147.8 (C(4)); 160.0 (C=N)); 163.0 (C=N). HR-MS: 577.1475 ($[M+H]^+$, $C_{29}H_{30}BrN_4O_4^+$; calc. 577.1450).

2-Bromo-N-*{5-[(5α,7α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-benzenamine* (**7n**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from EtOH. Yield 0.225 g (78%). M.p. 106–107°. IR: 3208*w*, 3064*w*, 2934*w*. ^{1}H-NMR[1]): 9.56 (*s*, NH); 7.03–7.80 (*m*, H–C(3′), H–C(4′), H–C(5′), H–C(6′)); 6.64 (*d*, $J(1,2) = 8.2$, H–C(2)); 6.53 (*d*, $J(1,2) = 8.2$, H–C(1)); 5.61 (*d*, $J(18,19) = 8.7$, H–C(18)); 5.55 (*d*, $J(18,19) = 8.7$, H–C(19)); 4.89 (*s*, H_β–C(5)); 3.71 (*m*, H_β–C(7)); 3.70 (*s*, MeO–C(3)); 3.42 (*s*, MeO–C(6)); 3.21 (*d*, $J(9\alpha,10\alpha) = 6.3$, H_α–C(9)); 3.13 (*d*, $J(10\alpha,10\beta) = 18.7$, H_β–C(10)); 2.43–3.06 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10)); 2.30 (*s*, MeN); 1.69–2.25 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.47 (*dd*, $J(8\alpha,8\beta) = 12.9$, $J(7\beta,8\alpha) = 6.2$, H_α–C(8)). ^{13}C-NMR[1]): 22.2 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.8 (C(7)); 42.9 (C(14)); 43.6 (MeN); 45.5 (C(16)); 46.9 (C(13)); 51.5 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 81.1 (C(6)); 91.0 (C(5)); 113.8 (C(2)); 119.9 (C(1)); 123.4 (C(5′)); 125.8 (C(6′)); 127.4 (C(18)); 128.6 (C(12)); 128.9 (C(4′)); 133.1 (C(2′)); 133.5 (C(3′)); 134.4 (C(11)); 137.0 (C(19)); 137.6 (C(1′)); 141.7 (C(3)); 147.8 (C(4)); 160.4 (C=N); 161.4 (C=N). HR-MS: 577.1436 ($[M+H]^+$, $C_{29}H_{30}BrN_4O_4^+$; calc. 577.1450).

N-*{5-[(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-4-iodobenzenamine* (**7o**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from EtOH. Yield 0.178 g (57%). M.p. 178–179°. IR: 3258*w*, 3055*w*, 2929*m*. ^{1}H-NMR[1]): 10.54 (*s*, NH); 7.64 (*d*, $J(2',3') = 8.8$, H–C(3′,5′)); 7.38 (*d*, $J(2',3') = 8.9$, H–C(2′,6′)); 6.64 (*d*, $J(1,2) = 8.2$, H–C(2)); 6.54 (*d*, $J(1,2) = 8.2$, H–C(1)); 5.64 (*d*, $J(18,19) = 8.7$, H–C(18)); 5.57 (*d*, $J(18,19) = 8.7$, H–C(19)); 4.90 (*s*, H_β–C(5)); 3.76 (*dd*, $J(7\beta,8\beta) = 9.2$, $J(7\beta,8\alpha) = 6.2$, H_β–C(7)); 3.70 (*s*, MeO–C(3)); 3.42 (*s*, MeO–C(6)); 3.20 (*d*, $J(9\alpha,10\alpha) = 6.3$, H_α–C(9)); 3.14 (*d*, $J(10\alpha,10\beta) = 19.1$, H_β–C(10)); 2.46–3.06 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10)); 2.30 (*s*, MeN); 1.70–2.26 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.47 (*dd*, $J(8\alpha,8\beta) = 12.8$, $J(7\beta,8\alpha) = 6.2$, H_α–C(8)). ^{13}C-NMR[1]): 22.2 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.8 (C(7)); 42.9 (C(14)); 43.6 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.4 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 81.0 (C(6)); 84.9 (C(4′)); 90.9 (C(5)); 113.8 (C(2)); 119.6 (C(3′)); 119.9 (C(1)); 127.6 (C(18)); 128.6 (C(12)); 134.4 (C(11)); 137.1 (C(19)); 138.0 (C(2′)), 139.2 (C(1′)); 141.7 (C(3)); 147.8 (C(4)); 160.0 (C=N); 160.6 (C=N). HR-MS: 625.1307 ($[M+H]^+$, $C_{29}H_{30}IN_4O_4^+$; calc. 625.1312).

N-*{5-[(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-3-iodobenzenamine* (**7p**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from AcOEt/hexane. Yield 0.206 g (66%). M.p. 131–132°. IR: 3322*w*, 3034*w*, 2941*w*. ^{1}H-NMR[1]): 10.83 (*s*, NH); 8.07 (*s*, H–C(2′)); 7.05–7.62 (*m*, H–C(4′), H–C(5′), H–C(6′)); 6.64 (*d*, $J(1,2) = 8.2$, H–C(2)); 6.55 (*d*, $J(1,2) = 8.2$, H–C(1)); 5.54 (*d*, $J(18,19) = 8.7$, H–C(18)); 5.49 (*d*, $J(18,19) = 8.7$, H–C(19)); 4.92 (*s*, H_β–C(5)); 3.89 (*m*, H_β–C(7)); 3.79 (*s*, MeO–C(3)); 3.51 (*s*, MeO–C(6)); 3.20 (*d*, $J(9\alpha,10\alpha) = 6.2$,

H_α–C(9)); 3.14 (*d*, *J*(10α,10β) = 19.2, H_β–C(10)); 2.45–3.07 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10)); 2.31 (*s*, MeN); 1.72–2.26 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.47 (*dd*, *J*(8α,8β) = 12.8, *J*(7β,8α) = 6.3, H_α–C(8)). ^{13}C-NMR[1]): 22.1 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.8 (C(7)); 42.9 (C(14)); 43.5 (MeN); 45.5 (C(16)); 47.0 (C(13)); 51.4 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 80.9 (C(6)); 90.9 (C(5)); 92.4 (C(3′)); 113.8 (C(2)); 116.3 (C(6′)); 119.5 (C(2′)); 119.9 (C(1)); 124.6 (C(4′)); 127.5 (C(18)); 128.6 (C(12)); 131.4 (C(5′)); 134.4 (C(11)); 137.1 (C(19)); 140.9 (C(1′)); 141.7 (C(3)); 147.8 (C(4)); 160.0 (C=N); 163.0 (C=N). HR-MS: 625.1322 ($[M+H]^+$, $C_{29}H_{30}IN_4O_4^+$; calc. 625.1312).

N-*{5-[(5α,7α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-1,3,4-oxadiazol-2-yl}-2-iodobenzenamine* (**7q**). Purified by CC (SiO_2, AcOEt/MeOH 9:1) and recrystallization from EtOH. Yield 0.203 g (65%). M.p. 110–111°. IR: 3299*w*, 3042*w*, 2929*w*. ^{1}H-NMR[1]): 9.40 (*s*, NH); 6.90–7.88 (*m*, H–C(3′), H–C(4′), H–C(5′), H–C(6′)); 6.63 (*d*, *J*(1,2) = 8.2, H–C(2)); 6.53 (*d*, *J*(1,2) = 8.2, H–C(1)); 5.60 (*d*, *J*(18,19) = 8.7, H–C(18)); 5.54 (*d*, *J*(18,19) = 8.7, H–C(19)); 4.87 (*s*, H_β–C(5)); 3.70 (*s*, MeO–C(3)); 3.68 (*m*, H_β–C(7)); 3.41 (*s*, MeO–C(6)); 3.21 (*d*, *J*(9α,10α) = 6.2, H_α–C(9)); 3.13 (*d*, *J*(10α,10β) = 18.6, H_β–C(10)); 2.44–3.06 (*m*, H_β–C(8), H_{eq}–C(16), H_α–C(10)); 2.30 (*s*, MeN); 1.68–2.26 (*m*, H_{ax}–C(16), H_{ax}–C(15), H_{eq}–C(15)); 1.50 (*dd*, *J*(8α,8β) = 12.3, *J*(7β,8α) = 6.2, H_α–C(8)). ^{13}C-NMR[1]): 22.2 (C(10)); 31.4 (C(15)); 33.0 (C(8)); 33.8 (C(7)); 42.9 (C(14)); 43.6 (MeN); 45.5 (C(16)); 46.9 (C(13)); 51.5 (*Me*O–C(6)); 56.4 (*Me*O–C(3)); 59.6 (C(9)); 81.1 (C(6)); 91.0 (C(5)); 95.1 (C(2′)); 113.8 (C(2)); 119.9 (C(1)); 124.2 (C(5′)); 126.9 (C(6′)); 127.4 (C(18)); 128.6 (C(12)); 134.4 (C(11)); 135.7 (C(1′)); 137.0 (C(19)); 137.1 (C(4′)); 139.9 (C(3′)); 141.7 (C(3)); 147.8 (C(4)); 160.1 (C=N); 161.4 (C=N). HR-MS: 625.1331 ($[M+H]^+$, $C_{29}H_{30}IN_4O_4^+$; calc. 625.1312).

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