# Formic Acid Catalyzed Rearrangement of Thevinols (=4,5-Epoxy-3,6-dimethoxy-$\alpha$,17-dimethyl-6,14-ethenomorphinan-7-methanols) and Their Vinylogous Analogues: Effects of 5$\beta$-Methyl Substitution

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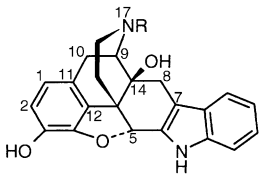
In a limited number of cases, 14-alkenylcodeinones (=14-alkenyl-7,8-didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-ones) can be obtained by formic acid treatment of thevinols (=4,5-epoxy-3,6-dimethoxy-$\alpha$,17-dimethyl-6,14-ethenomorphinan-7-methanols), but under these conditions the equivalent 14-alkenyl-7,8-dihydrocodeinones undergo further rearrangement (*Scheme 1* and *Table*). Introduction of a 5$\beta$-methyl group allows the 18,19-dihydrothevinol precursors to be rearranged to 14-alkenyl-7,8-dihydrocodeinones, but similar manipulation of the vinylogues of these thevinols is generally unable to prevent full rearrangement to 5,14-bridged thebainone derivatives.

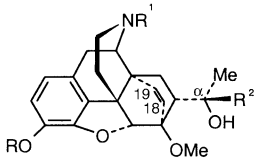
**Introduction.** – The indolomorphinan-3,14-diol structure **1** provided the first nonpeptide $\delta$-selective opioid receptor antagonist naltrindole (**1a**) and the selective $\delta$-partial agonist oxymorphindole (**1b**) [1][2]. Following investigations of 14-(alkylamino) and 14-(acylamino) derivatives [3], our interest in 14-substituted indolomorphinan-3-ols turned to 14-alkyl derivatives, of which only one **6a** has been reported (**6a** = NIH 10889); it had high affinity for $\delta$-opioid receptors and good selectivity for $\delta$ over $\mu$ and $\kappa$ [4].

The thevinols (=4,5-epoxy-3,6-dimethoxy-$\alpha$,17-dimethyl-6,14-ethenomorphinan-7-methanols) **2**, orvinols **3**, and their 18,19-dihydro analogues **4** and **5** are important series of opioid ligands from which etorphine (**3a**), a veterinary immobilizing agent, and buprenorphine (**5b**), a clinical analgesic and agent for treatment of opioid abuse, have been developed [5][6]. The 14-alkenylcodeinones (=14-alkenyl-7,8-didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-ones) **9** (see below, *Scheme 1*), which were among several sets of acid-catalyzed-rearrangement products of the thevinols **7** [7][8], provided the precursor **9c** for **6a** and also the precursor **9a** for the 3-methoxyindolomorphinan **6b** [9]. Though other syntheses of 14-alkyl-7,8-dihydrocodeinones have been reported [10][11], they are long and low-yielding. From the reaction of thevinols with formic acid, only three alkenylcodeinones, **9a**–**c**, have been reported [7][12], so that opportunities for the synthesis of 14-alkylindolomorphinans have been limited.

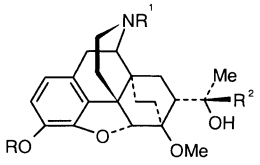
The major problem limiting the availability of stable 14-alkenylcodeinones is that they are prone to further acid-catalyzed rearrangement, which, in the case of the 7,8-dihydrocodeinone analogues **15** (see *Scheme 1*), prohibits their isolation; the products of formic acid treatment of the dihydrothevinols **13b**,**c** were 5,14-bridged dihydrothebainone derivatives **17b**,**c** (see *Scheme 1*) [7]. We hypothesized that introduction of a 5$\beta$-methyl group into the dihydrothevinols such as in **14a**–**c** should suppress cyclization



**1a** R=CPM
**b** R=Me

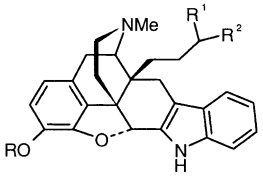


**2** R=Me
**3** R=H

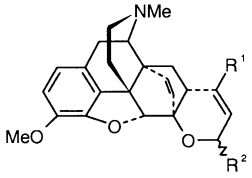


**4** R=Me
**5** R=H

**a** $R^1$=Me, $R^2$=$^n$Pr
**b** $R^1$=CPM, $R^2$=$^t$Bu
**c** $R^1$=Me, $R^2$=H



**6a** R=H, $R^1$=$R^2$=Me
**b** R=Me, $R^1$=H, $R^2$=Ph



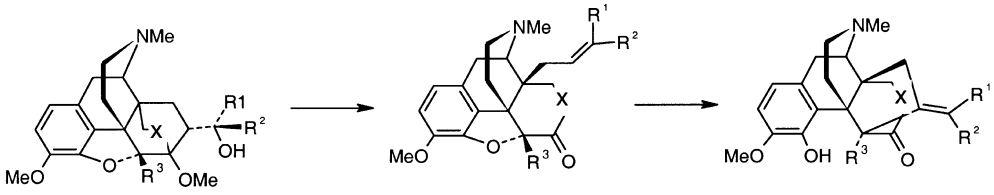
**19a** $R^1$=Me, $R^2$=H
**b** $R^1$=H, $R^2$=Me

CPM = cyclopropylmethyl

of the 14-alkenyl side chain to C(5) and allow the isolation of the 14-alkenyldihydrocodeinones **16a–c** rather than **18a–c** (*Scheme 1*).

The only other thevinol to have produced an alkenylcodeinone structure is vinylthevinol **7d**, giving in this case the 14-dienylcodeinone **9d** on brief heating with formic acid. This base was rapidly converted in cold 2N HCl to the furanocodide **19a** and, in hot HCl solution, to the bridged thebainone derivative **11d** [13] (*Scheme 1*). It was, thus, of interest to prepare further examples of the vinylthevinols, particularly the secondary alcohol analogue, in the hope of giving access to a range of 14-

*Scheme 1*[a])



**7** X = CH=CH, $R^3$=H
**8** X = CH=CH, $R^3$=Me
**13** X = $CH_2CH_2$, $R^3$=H
**14** X = $CH_2CH_2$, $R^3$=Me

**9** X = CH=CH, $R^3$=H
**10** X = CH=CH, $R^3$=Me
**15** X = $CH_2CH_2$, $R^3$=H
**16** X = $CH_2CH_2$, $R^3$=Me

**11** X = CH=CH, $R^3$=H
**12** X = CH=CH, $R^3$=Me
**17** X = $CH_2CH_2$, $R^3$=H
**18** X = $CH_2CH_2$, $R^3$=Me

**a** $R^1$ = H, $R^2$ = Ph; **b** $R^1$ = Me, $R^2$ = Ph; **c** $R^1$ = $R^2$ = Me; **d** $R^1$ = Me, $R^2$ = $CH_2$=CH; **e** $R^1$ = H, $R^2$ = $CH_2$=CH; **f** $R^1$ = H, $R^2$ = MeCH=CH; **g** $R^1$ = H, $R^2$ = $Me_2C$=CH; **h** $R^1$ = H, $R^2$ = PhCH=CH; **i** $R^1$ = Ph, $R^2$ = H

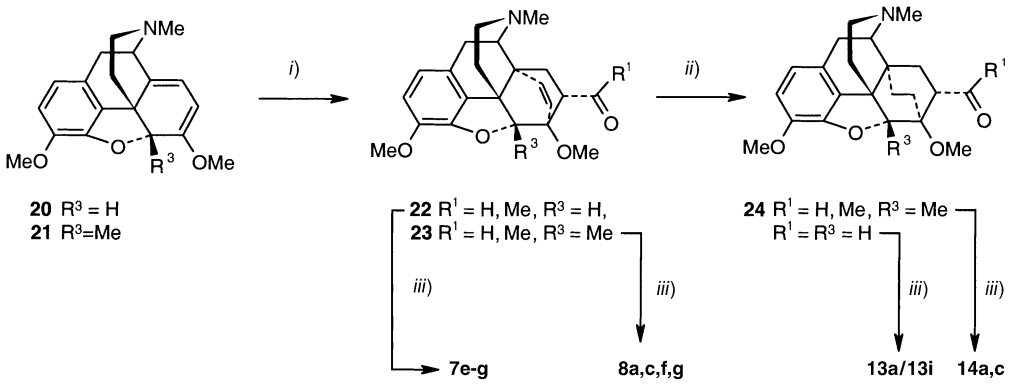
[a]) See *Table* for obtained products.

dienylcodeinones and, thence, to 14-alkyldihydrocodeinones. Again, for this purpose, 14$\beta$-methyl-substituted thevinols **8** should give precursors **10** rather than the bridged **12** (*Scheme 1*).

**Results and Discussion.** – *Scheme 2* shows the chemistry used for the preparation of the new thevinols and thevinol analogues. The starting materials were thebaine ((5$\alpha$)-6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methylmorphinan; **20**) and 5$\beta$-methylthebaine (**21**) [14], which were treated with prop-2-enal to give the *Diels–Alder* adducts **22** ($R^1$ = H) and **23** ($R^1$ = H). Analogous *Diels–Alder* reactions with methyl vinyl ketone afforded **22** ($R^1$ = Me) and **23** ($R^1$ = Me) [15]. Adducts **22** ($R^1$ = H) and **23** ($R^1$ = H, Me) were hydrogenated to give the corresponding 18,19-dihydro derivatives **24**. Reaction of thevinone **22** ($R^1$ = Me) with *Grignard* reagents ($R^2$MgBr) was shown by *Bentley et al.* [16] to be stereoselective, giving single diastereoisomers **7** ($R^1$ = Me). Though similar stereoselectivity was claimed for the formation of the secondary thevinols **7** ($R^1$ = H) from the *Grignard* reaction with aldehyde **22** ($R^1$ = H), no experimental details were given [16]. In our hands, the reported general procedure with **24** ($R^1 = R^3$ = H) and PhMgBr gave approximately equal quantities of the diastereoisomers **13a** ($R^1 = R^3$ = H, $R^2$ = Ph) and **13i** ($R^1$ = Ph, $R^2 = R^3$ = H). However, we found that, by conducting the reaction of **23** or **24** at $-78°$, single diastereoisomers of the secondary alcohols, *i.e.* **7e–g**, **8a**,**c**,**f**,**g**, and **14a**,**c** were produced in moderate to very good yields (*Table*). Their configurations at the exocyclic C($\alpha$) were defined by analogy with the previous work [16]. The benzylidene-substituted secondary alcohols **7h** and **8h** were prepared from thevinones **22** and **23** (*Scheme 3*) by base-catalyzed condensation with benzaldehyde *via* the benzylidene ketones **25** and **26**, respectively, which were reduced by *L-Selectride*.

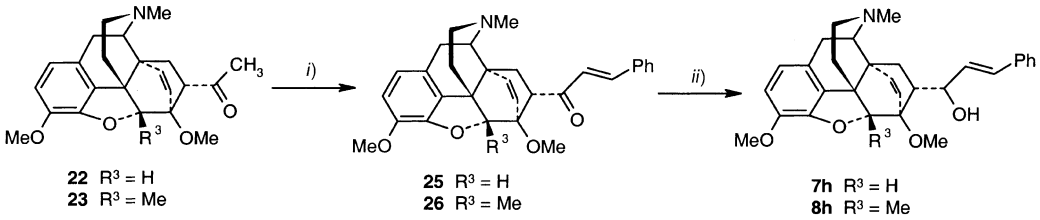
In the present investigation of the action of formic acid on the thevinols and analogues, the standard conditions used were to reflux the substrate with anhydrous formic acid until all had been transformed (TLC monitoring). This reaction time was eventually standardized as four hours. In the case of the secondary vinyl alcohol **7e**, the

*Scheme 2*




*i*) $CH_2$=CHCHO or $CH_2$=CHC(O)Me. *ii*) $H_2$, Pd/C. *iii*) $R^2$MgBr or PhLi.

*Scheme 3*




**22** $R^3$ = H
**23** $R^3$ = Me

**25** $R^3$ = H
**26** $R^3$ = Me

**7h** $R^3$ = H
**8h** $R^3$ = Me

*i*) LDA, $C_6H_5CHO$. *ii*) *L-Selectride.*

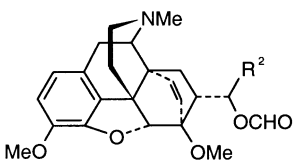
Table. *Yields of Thevinols* **7**, **8**, *and* **14** *from Thevinals and of Products from Their Treatment with Formic Acid*

| Thevinols[a]) | | | | Yield [%] | Product(s)[b]) | | | | Yield [%] |
|---|---|---|---|---|---|---|---|---|---|
| | $R^1$ | $R^2$ | $R^3$ | | | $R^1$ | $R^2$ | $R^3$ | |
| **7e** | H | $CH_2$=CH | H | 56 | **27a** | $CH_2$=CH | – | – | 61 |
| **7f** | H | MeCH=CH | H | 84 | **11f** (**19b**) | H | MeCH=CH | H | 34 (29) |
| **7g** | H | $Me_2C$=CH | H | 81 | **11g** | H | $Me_2C$=CH | H | 59 |
| **7h** | H | PhCH=CH | H | [c]) | **11h** | H | PhCH=CH | H | 71 |
| **8f** | H | MeCH=CH | Me | 75 | **10f** | H | MeCH=CH | Me | 43 |
| **8g** | H | $Me_2C$=CH | Me | 81 | **12g** | H | $Me_2C$=CH | Me | 63 |
| **8h** | H | PhCH=CH | Me | [c]) | **12h** (**10h**) | H | PhCH=CH | Me | 42 (12) |
| **8a** | H | Ph | Me | 91 | **10a** | H | Ph | Me | 78 |
| **14a** | H | Ph | Me | 46 | **16a** | H | Ph | Me | 54 |
| **8c** | Me | Me | Me | 84 | **10c** | Me | Me | Me | 65 |
| **14c** | Me | Me | Me | 86 | **16c** | Me | Me | Me | 54 |

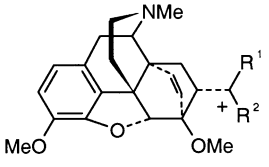
[a]) From thevinals. [b]) From thevinols and HCOOH. [c]) Formed by an alternative route, see *Scheme 3*.

only product was the formate ester **27a**. Though secondary thevinols, *e.g.*, **2c** and **4c**, gave only formate esters when reacted with formic acid [17], nepenthol (**7a**) was converted to nepenthene (**9a**) in good yield under these conditions [12] due to the ease of formation of the intermediate benzylic carbocation **28a**. A similar facilitation of ring opening of **7e** *via* the allylic carbocation **28b** might have been expected. The propenyl alcohol **7f** rearranged in the presence of formic acid to a mixture of the pyrano-derivative **19b** and the thebainone derivative **11f** (*Table*), isomeric with the rearrangement products **19a** and **11d** from vinylthevinol **7d** [13]. Further substitution of the vinyl group such as in **7g** increased the reactivity with formic acid resulting in conversion to the thebainone derivative **11g** in good yield; this also applied to the benzylidene analogue **7h** (*Table*). Thus, the secondary vinylogous thevinols **7e**–**h** proved not to be a good source of 14-dienylcodeinones **9e**–**h**. The only success in suppressing the formation of the 4-hydroxy derivatives in this series was in the case of the 5$\beta$-methyl-substituted propenyl alcohol **8f**, which gave 43% of the dienylcodeinone **10f**. The principal products from **8g** and **8h** were **12g** and **12h**, respectively, but, in the latter case, a small amount of the dienylcodeinone **10h** was also isolated (*Table*).

The 5$\beta$-methylnepenthol (**8a**) and 5$\beta$,20-dimethylthevinol (**8c**) gave with formic acid good yields of the 5$\beta$-methylalkenylcodeinones **10a** and **10c**, respectively, as




**27a** $R^2 = CH_2{=}CH_1$
**b** $R^2$ = Me




**28a** $R^1$ = H, $R^2$ = Ph
**b** $R^1$ = H, $R^2 = CH_2{=}CH$
**c** $R^1{=}R^2$= Me
**d** $R^1$ = H, $R^2 = Me_2C{=}CH$
**e** $R^1$ = H, $R^2$ = PhCH=CH

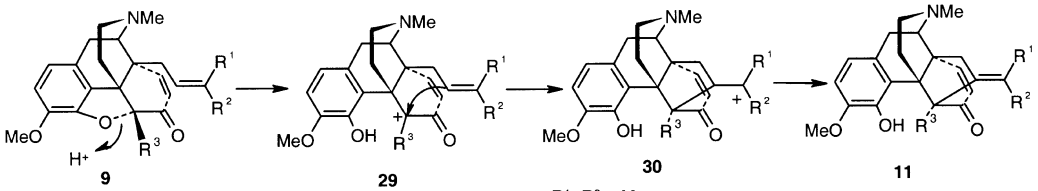
expected since nepenthol (**7a**) and methylthevinol (**7c**) behaved similarly [7][12]. However, the 18,19-dihydro analogues **14a** and **14c** both gave over 50% yields of the 5$\beta$-methylalkenyldihydrocodeinones **16a** and **16c** (*Table*), respectively, whereas **13a** and **13c** yielded only the 4-hydroxy derivatives **17a** and **17c**, respectively [7].

Comparison of the reactivity on formic acid treatment of the vinylogous thevinols **7f**–**h** with the equivalent thevinols **2c**, **7c** and **7a**, respectively, shows that the vinylogues are substantially more active. Whereas **2c** gave only the formate ester **27b** [17], **7f** was rearranged to **19b** and **11f**. Rearrangement of **7c** stopped at the alkenylcodeinone stage [7], whereas **7g** gave only the 4-hydroxy derivative **11g**, and comparison of **7a** with **7h** is similar. The greater reactivity of the vinylogues was also manifested in the 5$\beta$-methyl series where introduction of the 5-methyl group did not prevent formation of the 4-hydroxy derivatives **12g** and **12h** from **8g** and **8h**, respectively.

The product-determining factor in these rearrangements is the reactivity of the 14-alkenylcodeinones *vs.* the vinylogous dienylcodeinones. It was proposed by *Bentley et al.* [7] that conversion of the 14-alkenylcodeinones **9a**–**c** to the bridged thebainones **11a**–**c** was initiated by protonation of the epoxy O-atom followed by fission of the epoxy bridge and *Markownikov* addition of the C(5) carbocation **29** ($R^3 = H$) to the alkenyl-side-chain C=C bond (*Scheme 4*). The greater reactivity of the dienylcodeinones can, thus, be attributed to the greater migratory aptitude of the dienyl side chain in **9g**,**h** related to the greater stability of the 5,14-bridged carbocations **30b**,**d**.

The effect of introducing a 5$\beta$-methyl group into the alkenyl codeinones **9a**,**c** ($R^3$ = H) and dienylcodeinones **9b**,**d** ($R^3 = H$) on the reaction sequence shown in *Scheme 4*

*Scheme 4*




**a** $R^1{=}R^2$ = Me;
**b** $R^1$= H, $R^2$= $CH{=}CMe_2$;
**c** $R^1$= H, $R^2$= Ph;
**d** $R^1$= H, $R^2$= CH=CHPh

would not be inhibitory. Indeed, the tertiary carbocation **29** ($R^3 = Me$), if formed as a discrete species in the epoxy-bridge opening, would be stabilized compared to the secondary carbocation **29** ($R^3 = H$) formed from **9**, which would have a rate-enhancing effect. If however, the epoxy opening and formation of the 5,14-bridge were concerted processes, so that the new bridge was formed from the $\beta$-face as the epoxy bridge was fissioned, the steric inhibitory effect of the 5$\beta$-methyl group would be a greater factor. It is possible that the mechanisms for converting the dienylcodeinones and alkenylcodeinones into the bridged thebainones are different. The ionic mechanism in *Scheme 4* could be dominant for the more extensively conjugated dienyl series whereas for the alkenyl series the concerted mechanism could be of greater importance.

This view is supported by the effect of the 5$\beta$-methyl group in allowing the isolation of 14-alkenyldihydrocodeinones **16a** and **16c** from the acid-catalyzed rearrangement of the dihydrothevinols. It is evident that the factors governing acid-catalyzed rearrangements in these bridged-ring systems are very finely balanced.

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## Experimental Part

1. *General*. Anh. THF, DMF, $CH_2Cl_2$, and MeOH were purchased from *Aldrich*, HPLC-solvent-grade $CHCl_3$ and MeOH from *Merck*, and all other solvents used were GPR (general-purpose reagent) grade and from *Merck* or *Fisher Scientific*. Chemicals were purchased from *Aldrich*, *Fluka*, *Lancaster*, and *Across* chemical companies. Column chromatography (CC): silica gel *60* (35–70 μm); FC = flash chromatography. NMR Spectra: *Jeol 270* (270 ($^1$H) and 67.8 MHz ($^{13}$C)). *Jeol Lambda-300* (300 ($^1$H) and 75 MHz ($^{13}$C)), or *Jeol EX-400* (400 ($^1$H) and 101 MHz ($^{13}$C)) spectrometers; chemical shifts ($\delta$) in ppm, coupling constants $J$ in Hz. MS: electron ionization (EI) at 70 eV, *VG AutoSpec* instrument, equipped with a *Fisons* autosampler; HR = high resolution.

2. *Carboxaldehydes and Ketones* **22**–**24** *and Methanols* **13a**/**13i**. (*5α,6α,7α,14α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxaldehyde* (**22**; $R^1 = R^3 = H$). Thebaine (**20**; 2.5 g, 8.0 mmol), prop-2-enal (7.5 ml, 0.11 mol), and benzene (50 ml) were refluxed for 16 h. Benzene and unreacted prop-2-enal were evaporated and the crude white-yellow foam was purified by CC (MeOH/$CH_2Cl_2$ 95 : 5): **22** ($R^1 = H$) (quant.). Light yellow solid. $R_f$ (MeOH/$CH_2Cl_2$ 90 : 10) 0.69. IR ($CHCl_3$): 1722. $^1$H-NMR (270 MHz, $CDCl_3$): 1.48 (*dd*, *J* = 5.3, 13.1, $H_\alpha$–C(8)); 2.38 (*s*, MeN); 2.75 (*m*, $H_\beta$–C(7)); 2.83 (*dd*, *J* = 9.5, 13.1, $H_\beta$–C(8)); 3.61 (*s*, MeO–C(6)); 3.82 (*s*, MeO–C(3)); 4.64 (*d*, *J* = 1.4, H–C(5)); 5.58 (*d*, *J* = 8.6, H–C(19)); 5.88 (*d*, *J* = 8.6, H–C(18)); 6.55 (*d*, *J* = 8.2, H–C(1)); 6.64 (*d*, *J* = 8.2, H–C(2)); 9.41 (*d*, *J* = 3.8, CHO–C(7)). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 22.5; 26.6; 33.1; 42.9; 43.4; 45.4; 47.3; 49.7; 52.6; 56.5; 60.0; 80.8; 93.4; 113.4; 119.5; 126.6; 127.9; 133.6; 137.0; 141.9; 147.9; 201.6. EI-MS: 367 (100, $M^+$). HR-EI-MS: 367.1783 ($C_{22}H_{25}NO_4^+$; calc. 367.1783).

*(5α,6α,7α,14α)-4,5-Epoxy-18,19-dihydro-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxaldehyde* (**24**; $R^1 = R^3 = H$). A soln. of **22** ($R^1 = R^3 = H$) (1.31 g, 3.58 mmol) in EtOH (20 ml) was added to 10% Pd/C in EtOH (3 ml), and the mixture hydrogenated under 1 atm at r.t. for 1 h. The catalyst was removed by filtration through *Celite* and the solvent evaporated: **24** ($R^1 = R^3 = H$) (quant.). White solid. $R_f$ (AcOEt/hexane 7.2 : 2.5) 0.35, $R_f$ (MeOH/$CH_2Cl_2$ 90 : 10) 0.58. IR ($CHCl_3$): 1721s (CH=O). $^1$H-NMR (270 MHz, $CDCl_3$): 2.32 (*s*, MeN); 3.12 (*d*, *J* = 18.5, $H_\beta$–C(10)); 3.48 (*d*, *J* = 4.6, $H_\alpha$–C(9)); 3.51 (*s*, MeO–(6)); 3.88 (*s*, MeO–C(3)); 4.59 (*d*, *J* = 2.2, H–C(5)); 6.61 (*d*, *J* = 8.1, H–C(1)); 6.73 (*d*, *J* = 8.1, H–C(2)); 9.91 (*d*, *J* = 3.8, 1 H, CHO–C(7)). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 19.9; 22.0; 26.6; 28.5; 35.1; 35.5; 43.5; 45.2; 48.6; 51.6; 56.7; 61.4; 77.4; 92.2; 114.0; 119.3; 128.3; 132.1; 141.8; 146.7; 203.0. EI-MS: 369 (100, $M^+$). HR-EI-MS: 369.1936 ($C_{22}H_{27}NO_4^+$; calc. 369.1940).

*(αS,5α,6α,7α,14α)- and (αR,5α,6α,7α,14α)-4,5-Epoxy-18,19-dihydro-3,6-dimethoxy-17-methyl-α-phenyl-6,14-ethenomorphinan-7-methanol* (**13a** and **13i**, resp.). At r.t., **24** ($R^1 = R^3 = H$) (1.30 g, 3.54 mmol) was treated with phenylmagnesium bromide in toluene for 24 h. The crude product was purified by CC (MeOH/$CH_2Cl_2$ 98 : 2): **13i** (0.72 g, 45%) and **13a** (0.56 g, 35%).

*Data of* **13a**: $R_f$ (MeOH/$CH_2Cl_2$ 95:5) 0.63. IR ($CHCl_3$): 3401 (br., OH). $^1$H-NMR (270 MHz, $CDCl_3$): 2.17 (*s*, Me–N); 3.05 (*d*, *J* = 18.7, $H_\beta$–C(10)); 3.62 (*s*, MeO–C(6)); 3.88 (*s*, MeO–C(3)); 4.55 (*d*, *J* = 1.3, H–C(5)); 4.75 (*d*, *J* = 8.9, H–C(α)); 5.70 (*s*, OH–C(α)); 6.58 (*d*, *J* = 8.1, H–C(1)); 6.73 (*d*, *J* = 8.1, H–C(2)); 7.37 (*m*, Ph). $^{13}$C-NMR (67.8 MHz; $CDCl_3$): 17.7; 21.9; 32.2; 35.3; 41.8; 43.3; 45.1; 52.5; 56.8; 61.2; 70.2; 79.9; 94.8; 114.1; 115.3; 119.2; 125.3; 127.3; 128.1; 128.4; 129.3; 132.4; 141.8; 142.2; 146.6. EI-MS: 447 (88, $M^+$). HR-EI-MS: 447.2404 ($C_{28}H_{31}NO_4^+$; calc. 447.2409).

*Data of* **13i**: $R_f$ (MeOH/$CH_2Cl_2$ 5:95) 0.50. IR ($CHCl_3$): 3411 (br., OH–C(α)). $^1$H-NMR (270 MHz, $CDCl_3$): 2.28 (*s*, MeN); 3.05 (*d*, *J* = 18.7, $H_\beta$–C(10)); 3.51 (*s*, MeO–C(6)); 3.86 (*s*, MeO–C(3)); 4.20 (*d*, *J* = 2.0, H–C(5)); 5.92 (*s*, OH–C(α)); 6.58 (*d*, *J* = 8.1, H–C(1)); 6.74 (*d*, *J* = 8.1, H–C(2)); 7.35 (*m*, Ph). $^{13}$C-NMR (67.8 MHz; $CDCl_3$): 17.6; 20.3; 25.6; 32.2; 35.3; 35.9; 42.4; 43.4; 45.3; 50.9; 56.5; 61.1; 70.0; 79.9; 92.5; 113.6; 115.0; 118.9; 119.1; 126.8; 127.7; 128.0; 128.2; 132.0; 141.7; 144.8; 147.0. EI-MS: 447 (100, $M^+$). HR-EI-MS: 447.2402 ($C_{28}H_{31}NO_4^+$; calc. 447.2409).

*(5α,6α,7α,14α)-4,5-Epoxy-18,19-dihydro-3,6-dimethoxy-5,17-dimethyl-6,14-ethenomorphinan-7-carboxaldehyde* (**24**; $R^1$ = H, $R^3$ = Me). A mixture of (5α,6α,7α,14α)-4,5-epoxy-3,6-dimethoxy-5,17-dimethyl-6,14-ethenomorphinan-7-carboxaldehyde (**23**; $R^1$ = H, $R^3$ = Me) [18] (2.02 g, 7.04 mmol) in AcOEt (150 ml) and 10% Pd/C (0.51 g) was refluxed under 11 atm of $H_2$ for 30 h. After filtration over *Celite* and solvent evaporation, the residue was purified by recrystallization from EtOH: 1.04 g (51%) of **24** ($R^1$ = H, $R^3$ = Me). Solid. $R_f$ (AcOEt) 0.45. IR ($CHCl_3$): 1722. $^1$H-NMR (270 MHz, $CDCl_3$): 0.77 (*td*, *J* = 11.9, 3.4, 1 H); 1.06–1.27 (*m*, 2 H); 1.59 (*m*, $H_a$–C(8)); 1.65 (*s*, Me–C(5)); 1.85 (*m*, 1 H); 2.01–2.22 (*m*, 2 H); 2.24–2.56 (*m*, 4 H); 2.32 (*s*, MeN); 2.67–2.78 (*m*, H–C(7), $H_b$–C(8)); 3.10 (*d*, *J* = 9.5, 1 H); 3.47 (*s*, MeO–C(6)); 3.85 (*s*, MeO–C(3)); 6.56 (*d*, *J* = 8.0, H–C(1)); 6.71 (*d*, *J* = 8.2, H–C(2)); 9.98 (*s*, CHO–C(7)). $^{13}$C-NMR (75 MHz, $CDCl_3$): 16.3; 19.3; 22.2; 25.6; 28.0; 29.5; 36.8; 43.4; 45.1; 46.3; 51.5; 52.5; 56.6; 61.9; 78.9; 98.2; 113.5; 118.8; 128.7; 133.4; 141.3; 145.5; 204.8 (*C*HO–C(7)). EI-MS: 383 (50, $M^+$). HR-EI-MS: 383.2081 ($C_{23}H_{29}NO_4^+$; calc. 383.2096).

*1-[(5α,6α,7α,14α)-4,5-Epoxy-18,19-dihydro-3,6-dimethoxy-5,17-dimethyl-6,14-ethenomorphinan-7-yl]ethanone* (**24**; $R^1$ = $R^3$ = Me). A suspension of 3.3 g (8.4 mmol) 1-[(5α,6α,7α,14α)-4,5-epoxy-3,6-dimethoxy-5,17-dimethyl-4,5-epoxy-6,14-ethenomorphinan-7-yl]ethanone [18] (**23**; $R^1$ = $R^3$ = Me) and 10% Pd/C (1.78 g) in EtOH (100 ml) was hydrogenated at 50° and 60 psi for 2 days. The catalyst was removed by filtration over *Celite* and the crude mixture purified by FC (AcOEt/$CH_2Cl_2$ gradient): 2.63 g (77%) of **24** ($R^1$ = $R^3$ = Me). Solid. $R_f$ (AcOEt) 0.26. IR (film): 1712. $^1$H-NMR (270 MHz, $CDCl_3$): 0.71 (*m*, 1 H); 1.32–1.44 (*m*, 2 H); 1.59 (*dd*, *J* = 13.0, 2.4, 1 H); 1.65 (*s*, Me–C(5)); 1.70 (*dd*, *J* = 17.8, 4.6, 1 H); 1.74 (*m*, 1 H); 2.08 (*m*, 1 H); 2.22–2.33 (*m*, 2 H); 2.24 (*s*, 3 H); 2.28 (*s*, 3 H); 2.45–2.54 (*m*, 2 H); 2.68 (*d*, *J* = 6.6, 1 H); 3.07–3.16 (*m*, 2 H); 3.37 (*s*, 3 H); 3.85 (*s*, 3 H); 6.55 (*d*, *J* = 8.2, H–C(1)); 6.70 (*d*, *J* = 8.3, H–C(2)). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 16.27; 17.56; 22.30; 28.57; 29.77; 29.8; 34.17; 36.69; 43.43; 45.33; 46.97; 50.53; 52.21; 56.62; 61.89; 78.87; 98.49; 113.50; 118.74; 129.12; 133.63; 141.39; 145.66; 211.90 (*C*$OCH_3$). EI-MS: 397 (100, $M^+$). HR-EI-MS: 397.2252 ($C_{24}H_{31}NO_4^+$; calc. 397.2253).

3. *General Procedure for the Synthesis of the Alcohols* **7**, **8**, *and* **14** *Required as Starting Materials for the Acid-Catalyzed Rearrangements: (αS,5α,6α,7α,14α)-4,5-Epoxy-3,6-dimethoxy-5,17-dimethyl-α-phenyl-6,14-ethenomorphinan-7-methanol* (**8a**). A soln. of 1.7M PhLi in cyclohexane (5.0 ml, 8.5 mmol) was added to a stirred soln. of (5α,6α,7α,14α)-4,5-epoxy-3,6-dimethoxy-5,17-dimethyl-6,14-ethenomorphinan-7-carboxaldehyde (**23**; $R^1$ = H, $R^3$ = Me) (0.68 g, 1.7 mmol) at −78° in anh. THF (35 ml), and the mixture was allowed to warm to r.t. within 16 h. The volatiles were removed *in vacuo*, and the residue was purified by FC (AcOEt/$CH_2Cl_2$ gradient). 701 mg (91%) of **8a** as a single isomer ($^1$H-NMR). $R_f$ (AcOEt) 0.57. IR (film): 3445. $^1$H-NMR (270 MHz, $CDCl_3$, selected signals): 1.29 (*dd*, *J* = 11.9, 5.3, 1 H); 1.63 (*s*, Me–C(5)); 1.89 (*td*, *J* = 12.5, 5.9, 1 H); 2.29 (*s*, MeN); 3.09 (*d*, *J* = 6.6, 1 H); 3.21 (*d*, *J* = 18.5, 1 H); 3.80 (*s*, 3 H); 3.81 (*s*, 3 H); 5.27 (*d*, *J* = 1.3, CH–C(7)); 5.46 (*d*, *J* = 8.9, H–C(19)); 6.10 (*d*, *J* = 8.9, H–C(18)); 6.46 (*d*, *J* = 8.3, H–C(1)); 6.61 (*d*, *J* = 8.3, H–C(2)); 7.11–7.28 (*m*, Ph). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 16.26; 22.59; 24.89; 29.18; 43.39; 44.16; 45.54; 46.26; 48.43; 54.74; 56.76; 60.55; 71.08; 82.33; 100.36; 113.52; 118.74; 125.34; 125.91; 126.51; 127.98; 128.76; 135.64; 136.76; 141.44; 143.79. EI-MS: 459 (62, $M^+$), 352 (100). HR-EI-MS: 459.2423 ($C_{28}H_{33}NO_4^+$; calc. 459.2410).

*(αS,5α,6α,7α,14α)-4,5-Epoxy-18,19-dihydro-3,6-dimethoxy-5,17-dimethyl-α-phenyl-6,14-ethenomorphinan-7-methanol* (**14a**) [18]. From PhLi and (5α,6α,7α,14α)-4,5-epoxy-18,19-dihydro-3,6-dimethoxy-5,17-dimethyl-6,14-ethenomorphinan-7-carboxaldehyde (**24**; $R^1$ = H, $R^3$ = Me): **14a** (46%). $R_f$ (AcOEt) 0.59. IR ($CHCl_3$): 3437. $^1$H-NMR (400 MHz, $CDCl_3$): 0.69 (*m*, 1 H); 1.26 (*m*, 1 H); 1.51 (*m*, 1 H); 1.55 (*s*, Me–C(5)); 1.70 (*m*, 1 H); 1.76 (*m*, 2 H); 1.95 (*td*, *J* = 12.7, 5.9, 1 H); 2.08 (*dd*, *J* = 11.7, 5.9, 1 H); 2.18–2.29 (*m*, 3 H); 2.26 (*s*, MeN); 2.38 (*m*, 1 H); 2.65 (*d*, *J* = 6.4, 1 H); 3.07 (*d*, *J* = 18.1, 1 H); 3.53 (*s*, 3 H); 3.86 (*s*, 3 H); 5.37 (*s*, CH–C(7)); 6.52 (*d*, *J* = 7.9, H–C(1)); 6.69 (*d*, *J* = 8.3, H–C(2)); 7.18–7.38 (*m*, Ph). $^{13}$C-NMR (101 MHz,

$CDCl_3$): 16.32; 18.56; 22.26; 25.80; 29.21; 29.81; 37.02; 43.45; 45.14; 45.43; 46.82; 52.46; 56.72; 62.18; 70.90; 77.97; 99.51; 113.5; 118.44; 125.89; 126.71; 128.15; 129.30; 133.95; 141.27; 145.59; 146.03. EI-MS: 461 (85). HR-EI-MS: 461.2561 ($C_{29}H_{35}NO_4^+$; 461.2566).

*(*αR*,5*α*,6*α*,7*α*,14*α*)-4,5-Epoxy-*α*-ethenyl-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-methanol* (**7e**). From ethenylmagnesium bromide and (5α,6α,7α,14α)-4,5-epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-carboxaldehyde (**22**; $R^1 = R^3 = H$): **7e** (56%). $R_f$ (AcOEt) 0.39. IR (film): 3458. $^1$H-NMR (270 MHz, $CDCl_3$): 1.14 (*dd*, *J* = 12.9, 7.3, 1 H); 1.84 (*m*, 1 H); 1.99 (*m*, 1 H); 2.06 (*m*, 1 H); 2.31–2.56 (*m*, 3 H); 2.37 (*s*, MeN); 2.76 (*dd*, *J* = 12.8, 9.2, 1 H); 3.14–3.25 (*m*, 2 H); 3.66 (*s*, 3 H); 3.82 (*s*, 3 H); 4.35 (*m*, CH–C(7)); 4.56 (*d*, *J* = 1.0, H–C(5)); 5.06 (*dt*, *J* = 10.6, 1.7, $H_{trans}$ of $CH_2$=CH); 5.20 (*ddd*, *J* = 17.2, 2.0, 1.7, $H_{cis}$ of $CH_2$=CH) 5.45 (*d*, *J* = 8.9, H–C(19)); 5.79 (*ddd*, *J* = 17.2, 10.6, 5.3, $CH_2$=C*H*); 5.86 (*d*, *J* = 8.6, H–C(18)); 6.51 (*d*, *J* = 8.3, H–C(2)); 6.62 (*d*, *J* = 7.9, H–C(1)). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 22.35; 26.92; 33.64; 42.53; 42.98; 43.54; 45.59; 47.43; 53.61; 56.78; 60.07; 71.71; 81.54; 96.30; 113.79; 114.56; 119.27; 126.37; 128.38; 134.2; 135.78; 138.90; 141.84; 148.29. EI-MS: 395 (43). HR-EI-MS: 395.2104 ($C_{24}H_{29}NO_4^+$; calc. 395.2097).

*(*αR*,5*α*,6*α*,7*α*,14*α*)-4,5-Epoxy-3,6-dimethoxy-17-methyl-α-(prop-1-enyl)-6,14-ethenomorphinan-7-methanol* (**7f**). From (prop-1-enyl)magnesium bromide and **22** ($R^1 = R^3 = H$): **7f** (84%), 1:1 mixture of (*E*)- and (*Z*)-isomers. $R_f$ (AcOEt) 0.28. $^1$H-NMR (400 MHz, $CDCl_3$; selected signals): 1.67 (*m*, 3 H); 3.38 (*s*, 3 H); 3.65, 3.69 (2*s*, 3 H); 3.82 (*s*, 3 H); 4.31, 4.72 (2*m*, 1 H); 4.56, 4.57 (2*s*, 1 H); 5.44, 5.45 (2*d*, *J* = 8.8, H–C(19)); 5.84, 5.85 (2*d*, *J* = 8.8, H–C(18)); 6.52 (*d*, *J* = 8.3, H–C(1)); 6.62 (*d*, *J* = 8.3, H–C(2)). $^{13}$C-NMR (101 MHz, $CDCl_3$): 13.39; 17.74; 22.26; 26.77; 26.98; 33.57; 33.64; 42.55; 42.59; 42.89; 42.94; 43.52; 45.57; 47.38; 53.34; 53.41; 56.63; 60.01; 60.03; 66.20; 71.36; 81.35; 81.59; 95.88; 113.49; 119.20; 125.39; 126.11; 126.41; 126.46; 128.3; 131.15; 131.82; 134.13; 135.63; 135.86; 141.74; 141.76; 148.20. EI-MS: 409 (100, $M^+$), 338 (58). HR-EI-MS: 409.2253 ($C_{25}H_{31}NO_4^+$; calc. 409.2253).

*(*αR*,5*α*,6*α*,7*α*,14*α*)-4,5-Epoxy-3,6-dimethoxy-17-methyl-α-(2-methylprop-1-enyl)-6,14-ethenomorphinan-7-methanol* (**7g**). From (2-methylprop-1-enyl)magnesium bromide and **22** ($R^1 = R^3 = H$): **7g** (81%). $R_f$ (AcOEt) 0.34. IR (film): 3484. $^1$H-NMR (270 MHz, $CDCl_3$): 1.67–1.69 (*m*, $Me_2C$); 1.83 (*m*, 1 H); 1.94–2.08 (*m*, 2 H); 2.34–2.47 (*m*, 2 H); 2.40 (*s*, MeN); 2.54 (*m*, 1 H); 2.76 (*dd*, *J* = 12.7, 9.4, 1 H); 3.17–3.26 (*m*, 2 H); 3.67 (*s*, 3 H); 3.82 (*s*, 3 H); 4.58 (*d*, *J* = 1.0, 1 H); 4.66 (*d*, *J* = 8.9, 1 H); 5.17 (*d*, *J* = 9.2, 1 H); 5.46 (*d*, *J* = 8.9, H–C(19)); 5.84 (*d*, *J* = 8.9, H–C(18)); 6.53 (*d*, *J* = 7.9, H–C(1)); 6.63 (*d*, *J* = 7.9, H–C(2)). $^{13}$C-NMR (101 MHz, $CDCl_3$): 18.36; 22.33; 25.96; 26.70; 33.64; 42.54; 43.02; 43.59; 45.68; 47.43; 53.19; 56.67; 60.15; 67.08; 81.35; 95.54; 113.49; 119.23; 125.65; 126.75; 128.31; 133.97; 134.19; 135.79; 141.84; 148.29. EI-MS: 423 (100, $M^+$). HR-EI-MS: 423.2410 ($C_{26}H_{33}NO_4^+$; calc. 423.2410).

*(*αR*,5*α*,6*α*,7*α*,14*α*)-4,5-Epoxy-3,6-dimethoxy-5,17-dimethyl-α-(2-methylprop-1-enyl)-6,14-ethenomorphinan-7-methanol* (**8g**). From (2-methylprop-1-enyl)magnesium bromide and **23** ($R^1 = H$, $R^3 = Me$): **8g** (81%). $R_f$ (AcOEt) 0.21. IR (film): 3419. $^1$H-NMR (270 MHz, $CDCl_3$, selected signals): 1.06 (*dd*, *J* = 12.9, 6.7, 1 H); 1.60 (*s*, 3 H); 1.62 (*d*, *J* = 1.2, 3 H); 1.65 (*d*, *J* = 1.2, 3 H); 1.99 (*m*, 1 H); 2.16 (*m*, 1 H); 2.36 (*s*, MeN); 2.52 (*m*, 1 H); 2.73 (*m*, 1 H); 3.73 (*s*, 3 H); 3.78 (*s*, 3 H); 3.82 (*d*, *J* = 7.2, 1 H); 4.52 (*dd*, *J* = 9.4, 2.2, 1 H); 5.08 (*dt*, *J* = 9.4, 1.3, 1 H); 5.38 (*d*, *J* = 8.9, 1 H); 6.02 (*d*, *J* = 8.9, 1 H); 6.45 (*d*, *J* = 8.2, 1 H); 6.58 (*d*, *J* = 8.2, 1 H). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 16.26; 18.29; 22.52; 25.91; 26.88; 29.36; 43.48; 43.94; 44.14; 45.68; 48.38; 54.62; 56.62; 60.52; 68.46; 83.58; 100.40; 113.21; 118.63; 125.41; 125.99; 128.74; 133.44; 135.50; 135.67; 141.35; 147.54. EI-MS: 437 (65, $M^+$), 352 (100), 248 (99). HR-EI-MS: 437.2564 ($C_{27}H_{35}NO_4^+$; calc. 437.2566).

*(*αR*,5*α*,6*α*,7*α*,14*α*)-4,5-Epoxy-3,6-dimethoxy-5,17-dimethyl-α-(prop-1-enyl)-6,14-ethenomorphinan-7-methanol* (**8f**). From (prop-1-enyl)magnesium bromide and **23** ($R^1 = H$, $R^3 = Me$): **8f** (75%), 1:1 mixture of (*E*)- and (*Z*)-isomers. $R_f$ (AcOEt) 0.31. $^1$H-NMR (400 MHz, $CDCl_3$, selected signals): 1.61 (*m*, 3 H); 2.36 (*s*, 3 H); 3.72, 3.74 (2*s*, 3 H); 3.80 (*s*, 3 H); 4.19, 4.61 (2*m*, 1 H); 5.39 (*d*, *J* = 8.8, 1 H); 5.40 (*d*, *J* = 9.8, 1 H); 5.46, 5.51 (2*m*, 1 H); 6.01 (*d*, *J* = 8.8, 1 H); 6.02 (*d*, *J* = 9.3, 1 H); 6.47 (*d*, *J* = 8.3, 1 H); 6.58, 6.59 (2*d*, *J* = 8.3, 1 H). $^{13}$C-NMR (101 MHz, $CDCl_3$): 13.23; 16.14; 16.17; 17.63; 22.41; 22.43; 26.91; 27.09; 29.19; 29.27; 30.20; 43.35; 43.74; 43.79; 45.53; 48.23; 48.25; 54.47; 56.52; 60.37; 60.47; 67.41; 72.84; 83.62; 83.77; 100.18; 100.22; 113.16; 118.55; 118.57; 124.92; 125.20; 125.33; 125.42; 128.55; 131.39; 132.06; 135.21; 135.31; 135.34; 135.6; 141.22; 141.24; 147.39. EI-MS: 423 (51, $M^+$), 352 (70), 234 (100). HR-EI-MS: 423.2407 ($C_{26}H_{33}NO_4^+$; calc. 423.2410).

*(5*α*,6*α*,7*α*,14*α*)-4,5-Epoxy-3,6-dimethoxy-α,5,17-trimethyl-6,14-ethenomorphinan-7-methanol* (**8c**). From methylmagnesium bromide and **23** ($R^1 = R^3 = Me$) at r.t.: **8c** (84%). $R_f$ (AcOEt) 0.32. IR (film): 3494 (OH). $^1$H-NMR (270 MHz, $CDCl_3$): 0.77 (*dd*, *J* = 12.9, 7.6, 1 H); 0.99 (*s*, 3 H); 1.05 (*s*, 3 H); 1.67 (*s*, 3 H); 1.70 (*m*, 1 H); 1.96 (*dd*, *J* = 12.9, 5.9, 1 H); 2.17 (*d*, *J* = 8.4, 1 H); 2.32–2.45 (*m*, 2 H); 2.37 (*s*, MeN); 2.55 (*dd*, *J* = 11.6, 5.0, 1 H); 2.82 (*dd*, *J* = 12.9, 9.6, 1 H); 3.06 (*d*, *J* = 6.6, 1 H); 3.24 (*d*, *J* = 18.8, 1 H); 3.76 (*s*, 3 H); 3.79 (*s*, 3 H); 4.94 (*s*, 1 H); 5.36 (*d*, *J* = 8.9, 1 H); 6.01 (*d*, *J* = 8.9, 1 H); 6.48 (*d*, *J* = 8.0, 1 H); 6.61 (*d*, *J* = 8.2, 1 H). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 16.39; 22.47; 25.49; 28.79; 29.64; 30.72; 43.38; 43.76; 45.57; 47.77; 48.19; 54.58; 56.59; 60.39;

73.58; 86.11; 100.40; 113.27; 118.61; 124.84; 128.65; 134.50; 135.47; 141.28; 147.45. EI-MS: 412 (23), 411 (72), 353 (33), 352 (84), 222 (100). HR-EI-MS: 411.2426 ($C_{25}H_{33}NO_4^+$; calc. 411.2410).

*(5α,6α,7α,14α)-4,5-Epoxy-18,19-dihydro-3,6-dimethoxy-α-5,17-trimethyl-6,14-ethenomorphinan-7-methanolmorphinan* (**14c**). From methylmagnesium bromide and **24** ($R^1 = R^3 = Me$) at r.t.: **14c** (86%). $R_f$ (AcOEt) 0.29. IR (film): 3422. $^1$H-NMR (400 MHz, $CDCl_3$); 0.79 (*m*, 1 H); 1.24–1.42 (*m*, 2 H); 1.26 (*s*, 3 H); 1.36 (*s*, 3 H); 1.71 (*s*, 3 H); 1.97–2.07 (*m*, 3 H); 2.27 (*m*, 1 H); 2.55 (*m*, 1 H); 2.84–2.96 (*m*, 2 H); 3.04–3.11 (*m*, 2 H); 3.24 (*d*, *J* = 19.0, 1 H); 3.49–3.62 (*m*, 3 H); 3.52 (*s*, 3 H); 3.87 (*s*, 3 H); 4.87 (*s*, 1 H); 6.65 (*d*, *J* = 8.2, 1 H); 6.80 (*d*, *J* = 7.8, 1 H); 9.98 (br. *s*, 1 H). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 16.69; 17.62; 24.96; 25.39; 28.09; 30.15; 30.31; 32.44; 37.69; 42.90; 45.56; 46.21; 46.81; 52.18; 56.66; 63.62; 74.18; 81.22; 98.37; 114.97; 119.49; 123.87; 130.92; 142.59; 146.35. EI-MS: 414 (54), 413 (75), 419 (51), 380 (39), 355 (37), 354 (100). HR-EI-MS: 413.2572 ($C_{25}H_{35}NO_4^+$; calc. 413.2566).

4. *Alcohols* **7h** *and* **8h** *from* **25** *and* **26**, *resp. 1-[(5α,6α,7α,14α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-yl]-3-phenylprop-2-en-1-onae* (**25**). A soln. of **22** ($R^1 = Me$, $R^3 = H$) (1.18 g, 3.1 mmol) in anh. THF (25 ml) was added at −78° to a soln. of lithium diisopropylamide (LDA; 0.34 g, 3.2 mmol) in anh. THF (50 ml), and the mixture was allowed to warm to 0° within 2 h. Benzaldehyde (0.34 g, 3.2 mmol) was added to the soln. and the mixture was stirred overnight at r.t. The volatiles were evaporated, and the residue was purified by FC (AcOEt/$CH_2Cl_2$ 1:5): 598 mg (41%) of **25**. Colorless solid. $R_f$ (AcOEt) 0.81. IR (film): 1682. $^1$H-NMR (270 MHz, $CDCl_3$): 1.53 (*dd*, *J* = 19.5, 12.9, 1 H); 1.89 (*m*, 1 H); 2.05 (*m*, 1 H); 2.37 (*s*, MeN); 2.40–2.53 (*m*, 3 H); 2.99 (*dd*, *J* = 12.7, 9.4, 1 H); 3.19 (*dd*, *J* = 9.6, 6.6, 1 H); 3.21 (*m*, 1 H); 3.26 (*d*, *J* = 10.9, 1 H); 3.59 (*s*, 3 H); 3.83 (*s*, 3 H); 4.65 (*d*, *J* = 1.3, 1 H); 5.62 (*d*, *J* = 8.9, 1 H); 5.98 (*d*, *J* = 8.9, 1 H); 6.54 (*d*, *J* = 7.9, 1 H); 6.63 (*d*, *J* = 7.9, 1 H); 6.88 (*d*, *J* = 15.8, 1 H); 7.35–7.40 (*m*, 3 H); 7.51–7.57 (*m*, 3 H). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 22.52; 30.28; 33.58; 43.31; 43.51; 45.55; 47.46; 49.33; 53.65; 56.79; 60.08; 81.89; 95.64; 113.91; 119.39; 126.15; 126.38; 128.33; 128.77; 128.83; 130.20; 134.21; 134.91; 135.67; 141.77; 141.91; 148.19; 199.36. EI-MS: 470 (26), 469 (81), 454 (12), 338 (29), 311 (42), 294 (35), 131 (100), 103 (45). HR-EI-MS: 469.2246 ($C_{30}H_{31}NO_4^+$; calc. 469.2253).

*(αR,5α,6α,7α,14α)-4,5-Epoxy-3,6-dimethoxy-17-methyl-α-(2-phenylethenyl)-6,14-ethenomorphinan-7-methanol* (**7h**). A soln. of 1M *L-Selectride* in THF (0.75 ml, 0.75 mmol) was added at −78° to a soln. of **25** (347 mg, 0.73 mmol) in anh. THF (20 ml), and the mixture was stirred at −78° for 2 h. The mixture was treated with sat. $NH_4Cl$ soln. (10 ml) and extracted with $CHCl_3$ (3 × 10 ml). The combined org. extract was dried ($MgSO_4$) and evaporated and the residue purified by FC (AcOEt): 323 mg (91%) of **7h** as a single isomer ($^1$H-NMR). $R_f$ (AcOEt) 0.24. IR (film): 3425. $^1$H-NMR (270 MHz, $CDCl_3$): 0.89 (*m*, 1 H); 1.87 (*dd*, *J* = 12.9, 2.0, 1 H); 2.46 (*s*, MeN); 2.44–2.69 (*m*, 2 H); 2.84 (*dd*, *J* = 3.2, 9.3, 1 H); 3.18 (*d*, *J* = 18.9, 1 H); 3.16–3.27 (*m*, 2 H); 3.48 (*s*, 3 H); 3.70 (*s*, 3 H); 4.04 (*t*, *J* = 8.2, 1 H); 4.62 (*d*, *J* = 1.3, 1 H); 4.98 (br. *s*, 1 H); 5.54 (*d*, *J* = 8.9, 1 H); 5.99 (*d*, *J* = 8.6, 1 H); 6.12 (*dd*, *J* = 15.8, 7.6, 1 H); 6.50–6.58 (*m*, 2 H); 6.65 (*d*, *J* = 7.92, 1 H); 7.16–7.32 (*m*, 3 H); 7.38 (*m*, 2 H). EI-MS: 471 (100, $M^+$). HR-EI-MS: 472.2410 ($C_{30}H_{33}NO_4^+$; calc. 471.2422).

*1-[(5α,6α,7α,14α)-4,5-Epoxy-3,6-dimethoxy-5,17-dimethyl-6,14-ethenomorphinan-7-yl]-3-phenylprop-2-en-1-one* (**26**). As described for **25** with **23** ($R^1 = R^3 = Me$) and benzaldehyde: **26** (78%). $R_f$ (AcOEt) 0.35. IR (film): 1685. $^1$H-NMR (270 MHz, $CDCl_3$): 1.57 (*dd*, *J* = 13.0, 5.4, 1 H); 1.69 (*m*, 1 H); 1.73 (*s*, 3 H); 2.05 (*m*, 1 H); 2.35 (*s*, MeN); 2.39–2.61 (*m*, 3 H); 2.78 (*dd*, *J* = 12.7, 9.7, 1 H); 3.14–3.24 (*m*, 3 H); 3.61 (*s*, 3 H); 3.79 (*s*, 3 H); 5.54 (*d*, *J* = 8.9, 1 H); 6.05 (*d*, *J* = 8.9, 1 H); 6.50 (*d*, *J* = 8.2, 1 H); 6.62 (*d*, *J* = 8.2, 1 H); 6.85 (*d*, *J* = 16.1, 1 H); 7.33–7.38 (*m*, 3 H); 7.46 (*d*, *J* = 15.9, 1 H); 7.54 (*m*, 2 H). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 16.15; 22.61; 28.49; 28.98; 43.31; 44.05; 45.44; 48.09; 50.05; 54.53; 56.49; 60.46; 83.67; 99.6; 113.26; 118.58; 124.34; 127.52; 127.94; 128.45; 128.49; 129.70; 134.89; 135.11; 135.57; 140.43; 141.35; 147.19; 199.62. EI-MS: 483 (46, $M^+$), 294 (75), 131 (100). HR-EI-MS: 483.2399 ($C_{31}H_{33}NO_4^+$; calc. 483.2410).

*(αR,5α,6α,7α,14α)-4,5-Epoxy-3,6-dimethoxy-5,17-dimethyl-α-(2-phenylethenyl)-6,14-ethenomorphinan-7-methanol* (**8h**). As described for **7h**, with **26** and *L-Selectride:* **8h** 87%. $R_f$ (AcOEt) 0.37. IR (film): 3431. $^1$H-NMR (270 MHz, $CDCl_3$): 0.83 (*dd*, *J* = 13.4, 5.3, $H_a$–C(8)); 1.65 (*s*, Me–C(5)); 1.67 (*m*, $H_a$–C(16)); 2.01 (*ddd*, *J* = 12.8, 5.9, $H_b$–C(16)); 2.10 (*m*, $H_\beta$–C(7)); 2.31 (*s*, MeN); 2.34–2.42 (*m*, $H_a$–C(10), $H_a$–C(15)); 2.51 (*dd*, *J* = 11.4, 5.1, $H_b$–C(15)); 2.65 (*dd*, *J* = 13.4, 9.7, $H_b$–C(8)); 3.02 (*d*, *J* = 6.6, 1 H); 3.21 (*d*, *J* = 18.7, H–C(9)); 3.79 (*s*, 3 H); 3.81 (*s*, 3 H); 3.98 (*m*, CH–(7)); 5.36 (*s*, OH); 5.51 (*d*, *J* = 9.2, H–C(19)); 6.06–6.12 (*m*, H–C(18), PhCH=C*H*); 6.48–6.51 (*m*, H–C(1), PhC*H*=CH); 6.62 (*d*, *J* = 8.1, H–C(2)); 7.21 (*m*, 1 H); 7.29 (*m*, 2 H); 7.37 (*m*, 2 H). $^1$H,$^1$H-NOESY ($CDCl_3$, selected cross-peaks): 0.83 ($H_a$–C(8))/3.98 (CH–C(7)); 0.83 ($H_a$–C(8))/6.06–6.12 (H–C(18), PhCH=C*H*); 2.10 (*m*, $H_\beta$–C(7))/2.65 ($H_b$–C(8)); 2.65 ($H_b$–C(8))/6.06–6.12 (H–C(18), PhCH=C*H*); 3.98 (CH–C(7))/6.48–6.51 (H–C(1), PhC*H*=CH). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 16.52; 22.52; 28.91; 29.07; 43.43; 43.62; 44.24; 45.54; 47.71; 55.03; 56.58; 60.47; 76.30; 86.48; 100.14;

113.10; 118.92; 124.77; 126.58; 127.50; 128.42; 128.48; 129.91; 132.35; 135.68; 136.83; 136.87; 141.52; 147.00. EI-MS: 485 (75, $M^+$), 352 (100), 296 (93). HR-EI-MS: 485.2551 ($C_{31}H_{35}NO_4^+$; calc. 485.2566).

5. *General Procedure for the Acid-Catalyzed Rearrangements: (5α,14β)-7,8-Didehydro-4,5-epoxy-3-methoxy-5,17-dimethyl-14-[(2*E*,4*E*)-5-phenylpenta-2,4-dienyl]morphin-2-en-6-one* (**10h**) *and (5β,14β,18*E*)-7,8-Didehydro-4-hydroxy-3-methoxy-5,17-dimethyl-18-(3-phenylprop-2-enylidene)-5,14-ethanomorphinan-6-one* (**12h**) *from* **8h**. A soln. of **8h** (0.49 g, 1.0 mmol) in formic acid (5 ml) was heated to 100° for 4 h. After this time, most of the volatiles were evaporated. The residue was basified with ammonia and extracted with $CHCl_2$ (3 × 10 ml). The combined extract was washed with $H_2O$ (10 ml) and brine (10 ml) and dried ($MgSO_4$) and the crude mixture purified by FC (AcOEt/$CH_2Cl_2$ 1:5, then AcOEt gradient): 54 mg (12%) of **10h** and 190 mg (42%) of **12h**.

Data of **10h**: $R_f$ (AcOEt) 0.69. IR (film): 1678. $^1$H-NMR (270 MHz, $CDCl_3$, selected signals): 1.50 (*m*, 1 H); 1.70 (*s*, 3 H); 2.11 (*m*, 1 H); 2.37 (*s*, MeN); 2.60 (*m*, 1 H); 3.05–3.16 (*m*, 2 H); 3.78 (*s*, MeO–C(3)); 5.74 (*m*, 1 H); 6.06 (*d*, *J* = 10.4, H–C(8)); 6.25–6.80 (*m*, 9 H); 7.17–7.39 (*m*, 4 H). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 17.49 (*q*, *Me*–C(5)); 21.29 (*t*); 25.89 (*t*); 39.92 (*t*); 42.82 (*q*, MeN); 44.53 (*s*); 45.87 (*t*); 47.25 (*s*); 56.37; 58.85; 92.75 (*s*, C(5)); 113.31 (*d*); 119.25 (*d*); 126.20 (*d*); 126.36 (*d*); 126.46 (*d*); 127.44 (*s*); 127.57 (*d*); 128.58 (*d*); 128.70 (*d*); 131.44 (*d*); 132.65 (*s*); 134.76 (*d*); 137.16 (*s*); 142.00 (*s*); 143.85 (*s*); 155.50 (*d*, C(8)); 196.89 (*s*, C(6)). EI-MS: 453 (100, $M^+$). HR-EI-MS: 453.2305 ($C_{30}H_{31}NO_3^+$; calc. 453.2304).

*Data of* **12h**: $R_f$ (AcOEt) 0.58. IR (film): 3504, 1678. $^1$H-NMR (270 MHz, $CDCl_3$; selected signals): 1.90 (*s*, Me–C(5)); 2.11 (*td*, *J* = 12.2, 3.6, 1 H); 2.38 (*s*, MeN); 2.46 (*m*, 1 H); 2.78 (*dd*, *J* = 18.8, 5.9, 1 H); 3.26 (*d*, *J* = 18.5, 1 H); 3.80 (*s*, MeO–C(3)); 5.70 (*d*, *J* = 9.6, H–C(7)); 6.05 (*s*, OH–C(4)); 6.40 (*d*, *J* = 10.9, 2.0, PhCH=CHC*H*); 6.49 (*d*, *J* = 15.5, PhC*H*=CHCH); 6.59 (*d*, *J* = 8.6, H–C(2)); 6.62 (*d*, *J* = 8.3, H–C(1)); 6.76 (*d*, *J* = 9.9, H–C(8)); 6.85 (*dd*, *J* = 15.1, 10.9, PhCH=C*H*CH); 7.16–7.27 (*m*, Ph). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 15.04 (*q*, *Me*–C(5)); 25.81 (*t*); 29.51 (*t*); 33.47 (*t*); 42.99 (*q*, MeN); 46.04 (*t*, C(16)); 50.17 (*s*); 54.27 (*s*); 56.10; 56.42; 65.96 (C(5)); 108.33 (*d*); 118.33 (*d*); 126.30 (*s*); 126.35 (*d*); 126.65 (*d*); 127.35 (*d*); 128.33 (*d*); 128.59 (*d*); 128.84 (*d*); 132.01 (*s*); 132.16 (*d*); 137.69 (*s*); 143.66 (*s*); 144.69 (*s*); 146.64 (*s*); 153.35 (*d*, C(8)); 196.57 (*s*, C(6)). EI-MS: 453 (100, $M^+$). HR-EI-MS: 453.2304 ($C_{30}H_{31}NO_3^+$; calc. 453.2304) 453.2299.

*(α*R*,5α,6α,7α,14α)-4,5-Epoxy-α-ethenyl-3,6-dimethoxy-17-methyl-6,14-ethenomorphinan-7-methanol Formate* (**27a**) from **7e**. Yield 61 %. $R_f$ (AcOEt) 0.67. IR (film): 1723. $^1$H-NMR (270 MHz, $CDCl_3$): 1.85 (*m*, 1 H); 1.93–2.04 (*m*, 2 H); 2.31–2.62 (*m*, 3 H); 2.40 (*s*, MeN); 2.82 (*m*, 1 H); 3.18–3.25 (*m*, 2 H); 3.62 (*s*, 3 H); 3.82 (*s*, 3 H); 4.52 (*d*, *J* = 0.98, 1 H); 5.17 (*d*, *J* = 7.8, 1 H); 5.20 (*d*, *J* = 14.2, 1 H); 5.41 (*d*, *J* = 8.8, 1 H); 5.62–5.82 (*m*, 3 H); 6.52 (*d*, *J* = 8.3, H–C(1)); 6.62 (*d*, *J* = 8.3, H–C(2)); 7.99 (*s*, OCHO). $^{13}$C-NMR (75.5 MHz, $CDCl_3$): 22.39 (*t*); 26.69 (*t*); 33.49 (*t*); 41.00 (*d*); 42.62 (*s*); 43.52 (*q*); 45.63 (*t*); 47.09 (*s*); 53.23 (*q*); 56.64 (*q*); 60.11 (*d*); 72.18 (*d*); 79.63 (*s*); 95.81 (*d*, C(5)); 113.52 (*d*); 116.55 (*t*, CH=C$H_2$); 119.26 (*d*); 126.62 (*d*); 127.96 (*s*); 134.03 (*s*); 134.04 (*d*); 134.91 (*d*); 141.83 (*s*); 148.2 (*s*); 160.4 (*d*, O*C*HO). EI-MS: 423 (100, $M^+$), 338 (94), 248 (90). HR-EI-MS: 423.2043 ($C_{25}H_{29}NO_5^+$; calc. 423.2046).

*(5β,14β,18*E*)-7,8-Didehydro-4-hydroxy-3-methoxy-17-methyl-18-(3-methylbut-2-enylidene)-5,14-ethanomorphinan-6-one* (**11g**) *from* **7g**. Yield 59%. $R_f$ (AcOEt): 0.61. IR (film): 3268, 1678. $^1$H-NMR (270 MHz, $CDCl_3$): 1.27 (*m*, 1 H); 1.75 (*s*, 3 H); 1.78 (*s*, 3 H); 1.90 (*m*, 1 H); 2.05 (*m*, 1 H); 2.20 (*d*, *J* = 16.8, $H_a$–C(16)); 2.37 (*s*, MeN); 2.41 (*m*, 1 H); 2.71 (*m*, 1 H); 3.11–3.21 (*m*, 2 H); 3.42 (*m*, $H_b$–C(16)); 3.80 (*s*, MeO–(3)); 4.27 (*s*, H–C(5)); 5.69 (*dd*, *J* = 9.7, 1.5, H–C(7)); 5.73 (br. *s*, OH–C(4)); 5.84 (*d*, *J* = 11.5, $Me_2$C=C*H*CH); 6.55–6.64 (*m*, H–C(1), H–C(2), $Me_2$C=CHC*H*); 6.80 (*d*, *J* = 9.6, H–C(8)). $^1$H,$^1$H-NOESY ($CDCl_3$; selected cross-peaks): 2.20 ($H_a$–C(16))/5.84 ($Me_2$C=C*H*CH); 3.42 ($H_b$–C(16))/5.84 ($Me_2$C=C*H*CH); 4.27 (H–C(5))/6.55–6.64 (H–C(1), H–C(2), $Me_2$C=CHC*H*). $^{13}$C-NMR (101 MHz, $CDCl_3$): 18.35; 24.80; 26.28; 30.76; 32.37; 43.18; 45.91; 49.29; 49.55; 55.88; 56.60; 67.13 (*s*, C(5)); 108.44 (*d*, $Me_2$C=CH*C*H); 118.03 (*d*, C(2)); 122.46 (*d*, $Me_2$C=*C*HCH); 125.21 (*d*, C(1)); 125.69 (*s*); 128.52 (*d*, C(7)); 131.00 (*s*); 135.51 (*s*); 135.72 (*s*); 143.12 (*s*); 144.55 (*s*); 154.98 (*d*, C(8)); 196.94 (*s*, C(6)). EI-MS: 391 (100, $M^+$), 230 (71). HR-EI-MS: 391.2153 ($C_{25}H_{29}NO_3^+$; calc. 391.2147).

*(5β,14β,18*E*)-7,8-Didehydro-4-hydroxy-3-methoxy-17-methyl-18-(but-2-enylidene)-5,14-ethanomorphinan-6-one* (**11f**) *and (5α,6α,7α,14α)-6,7-Didehydro-6,7-dihydro-3-methoxy-6′,17-dimethyl-6′*H*-pyrano[2′,3′:6,7]-6,14-ethenomorphinan* (**19b**) *from* **7f**. *Data of* **11f**: Yield 34%. $R_f$ (AcOEt) 0.62. IR (film): 3432 (OH), 1673 (C=O). $^1$H-NMR (270 MHz, $CDCl_3$): 1.47 (*m*, 1 H); 1.75 (*m*, 3 H); 1.89 (*m*, 1 H); 2.05 (*m*, 1 H); 2.21 (*d*, *J* = 16.6, $H_a$–C(19)); 2.37 (*s*, MeN); 2.41 (*m*, 1 H); 2.71 (*m*, 1 H, $H_a$–C(10)); 3.11–3.19 (*m*, H–C(9), $H_b$–C(10)); 3.43 (*m*, $H_b$–C(19)); 3.78 (*s*, MeO–C(3)); 4.22 (*s*, H–C(5)); 5.62–5.73 (*m*, H–C(7), MeC*H*=CHCH); 5.75 (*s*, OH–C(4)); 6.08 (*ddd*, *J* = 15.1, 10.8, 1.5, MeCH=C*H*CH); 6.38 (*d*, *J* = 10.8, MeCH=CHC*H*); 6.56–6.62 (*m*, H–C(1), H–C(2)); 6.81 (*d*, *J* = 9.8, H–C(8)). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 18.38 (*q*, *Me*–C(5)); 24.76 (*t*, C(10)); 30.69 (*t*); 32.34 (*t*); 43.13 (*q*, MeN); 45.85 (*t*); 49.26 (*s*); 49.54 (*s*); 55.85 (*q*, MeO); 56.53 (*d*, C(9));

66.86 (*d*, C(5)); 108.45 (*d*, C(2)); 117.99 (*d*, C(1)); 125.59 (*s*); 128.51 (*d*); 128.66 (*d*); 128.88 (*d*); 129.40 (*d*); 130.93 (*s*); 136.06 (*s*); 143.08 (*s*); 144.52 (*s*); 154.93 (*d*, C(8)); 196.78 (*s*, C=O). EI-MS: 377 (100, $M^+$), 230 (54). HR-EI-MS: 377.1989 ($C_{24}H_{27}NO_3^+$; calc. 377.1991).

*Data of* **19b**: Yield 29%. $R_f$ (AcOEt) 0.57. $^1$H-NMR (400 MHz, $CDCl_3$): 0.94 (*dd*, *J* = 12.5, 6.9, H–C(8)); 1.36 (*d*, *J* = 6.9, Me–C(6)); 1.85 (*m*, 1 H); 2.00 (*dd*, *J* = 4.0, 2.0, 1 H); 2.23 (*m*, H–C(7)); 2.35–2.44 (*m*, 2 H); 2.37 (*s*, MeN); 2.51 (*m*, 1 H); 3.07–3.24 (*m*, $H_b$–C(8), H–C(9), $H_b$–C(10)); 3.83 (*s*, MeO–C(3)); 4.38 (*d*, *J* = 1.3, H–C(5)); 4.51 (*m*, H–C(6′)); 5.41 (*d*, *J* = 8.9, H–C(19)); 5.48 (*m*, H–C(5′)); 5.61 (*m*, H–C(4′)); 5.80 (*d*, *J* = 8.9, H–C(18)); 6.49 (*d*, *J* = 7.9, H–C(1)); 6.62 (*d*, *J* = 7.9, H–C(2)). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 22.34 (*t*, C(10)); 23.05 (*Me*–C(6′)); 32.41 (*d*, C(7)); 32.77 (*t*, C(8)); 33.57 (*t*); 42.68 (*s*); 43.58 (*q*, MeN), 45.67 (*t*); 46.92 (*s*); 56.93 (*q*, MeO–C(3)); 60.09 (*d*, C(9)); 68.65 (*d*, C(6′)); 76.62 (*s*); 96.74 (*d*, C(5)); 114.04 (C(2)); 118.93 (C(1)); 128.21 (*s*); 128.54 (C(5′)); 128.93 (C(4′)); 130.15 (C(18)); 134.51 (*s*); 135.73 (C(19)); 141.89 (*s*); 148.77 (*s*). EI-MS: 377 (100), 362 (29), 202 (78). HR-EI-MS: 377.1997 ($C_{24}H_{27}NO^{3+}$, calc. 377.1991).

*(5β,14β,18*E*)-7,8-Didehydro-4-hydroxy-3-methoxy-5,17-dimethyl-18-(3-methylbut-2-enylidene)-5,14-ethanomorphinan-6-one* (**12g**) *from* **8g**. Yield 63%. $R_f$ (AcOEt) 0.58. IR (film): 3511 (OH), 1678 (C=O). $^1$H-NMR (400 MHz, $CDCl_3$): 1.54 (*m*, 1 H); 1.75 (*s*, 3 H); 1.78 (*s*, 3 H); 1.82 (*m*, 1 H); 1.87 (*s*, 3 H); 2.05 (*td*, *J* = 12.2, 3.4, 1 H); 2.26 (*dd*, *J* = 16.6, 1.5, 1 H, $H_a$–C(16)); 2.37 (*s*, MeN); 2.42 (*m*, 1 H); 2.79 (*dd*, *J* = 18.6, 5.9, 1 H); 3.08 (*d*, *J* = 5.9, 1 H); 3.19 (*d*, *J* = 18.6, 1 H); 3.58 (*d*, *J* = 16.1, $H_b$–C(16)); 3.78 (*s*, MeO–C(3)); 5.67 (*d*, *J* = 9.3, H–C(7)); 5.87 (*m*, H–C(19)); 6.07 (br. *s*, OH–C(4)); 6.41 (*m*, H–C(18)); 6.57 (*d*, *J* = 8.3, H–C(1)); 6.62 (*d*, *J* = 7.8, H–C(2)); 6.72 (*d*, *J* = 9.8, H–C(8)). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 15.19 (*q*); 18.41 (*q*); 25.71 (*t*); 26.39 (*q*); 29.39 (*t*); 33.02 (*t*); 43.01 (*q*, MeN); 46.04 (*t*, C(16)); 50.02 (*s*); 54.14 (*s*); 56.00; 56.31; 65.51 (*s*, C(5)); 108.09 (*d*, C(2)); 118.21 (*d*, C(1)); 122.70 (*d*); 124.46 (*d*); 126.40 (*s*); 128.66 (*d*); 132.09 (*s*); 135.45 (*s*); 142.29 (*s*); 143.57 (*s*); 144.54 (*s*); 153.47 (C(8)); 197.22 (C(6)). EI-MS: 405 (100, $M^+$), 230 (56). HR-EI-MS: 405.2306 ($C_{26}H_{31}NO_3^+$; calc. 405.2304).

*(5α,14β)-4,5-Epoxy-3-methoxy-5,17-dimethyl-14-(3-methylbut-2-enyl)morphinan-6-one* (**16c**) *from* **14c**. Yield 54%. $R_f$ (AcOEt) 0.67. IR (film): 1720 (C=O). $^1$H-NMR (270 MHz, $CDCl_3$): 1.29 (*m*, 1 H); 1.41 (*m*, 1 H); 1.54 (*m*, 1 H); 1.63 (*s*, 3 H); 1.72 (*m*, 1 H); 1.74 (*s*, 3 H); 1.76 (*s*, 3 H); 2.11 (*m*, 1 H); 2.17–2.29 (*m*, 3 H); 2.31 (*s*, MeN); 2.51–2.62 (*m*, 2 H); 2.81 (*d*, *J* = 5.1, 1 H); 3.04 (*d*, *J* = 18.3, 1 H); 3.57 (*dd*, *J* = 14.1, 7.9, 1 H, $Me_2C$=CHC$H_2$); 3.88 (*s*, MeO–C(3)); 5.17 (*m*, $Me_2C$=C*H*$CH_2$); 6.58 (*d*, *J* = 8.1, H–C(1)); 6.65 (*d*, *J* = 8.1, H–C(2)). $^{13}$C-NMR (101 MHz, $CDCl_3$): 17.56 (*q*); 18.07 (*q*); 20.03 (*t*); 25.96 (*t*); 26.23 (*q*); 26.55 (*t*); 26.63 (*t*); 35.79 (*t*); 41.09 (*s*); 43.04 (*q*, MeN); 45.82 (*t*, C(16)); 49.88 (*s*); 56.39; 59.44; 95.46 (*s*, C(5)); 113.33 (*d*, C(2)); 119.00 (*d*); 119.44 (*d*); 126.86 (*s*); 131.18 (*s*); 134.79 (*s*); 142.42 (*s*); 144.40 (*s*); 212.36 (*s*, C(6)). EI-MS: 381 (100), 244 (99), 189 (39). HR-EI-MS: 381.2305 ($C_{24}H_{31}NO_3^+$; calc. 381.2304).

*(5α,14β)-7,8-Didehydro-4,5-epoxy-3-methoxy-5,17-dimethyl-14-(3-methylbut-2-enyl)morphinan-6-one* (**10c**) *from* **8c**. Yield: 65%. $R_f$ (AcOEt) 0.68. IR (film): 1678 (C=O). $^1$H-NMR (270 MHz, $CDCl_3$): 1.46 (*m*, 1 H); 1.66 (*s*, 3 H); 1.72 (*s*, 3 H); 1.73 (*s*, 3 H); 2.00 (*dd*, *J* = 12.9, 7.2, 1 H, $Me_2C$=CHC$H_2$); 2.19–2.31 (*m*, 3 H); 2.35 (*s*, MeN); 2.58 (*m*, 1 H); 3.07–3.12 (*m*, 2 H); 3.64 (*dd*, *J* = 12.5, 8.9, 1 H, $Me_2C$=CHC$H_2$); 3.79 (*s*, MeO–C(3)); 5.11 (*t*, *J* = 7.9, $Me_2C$=C*H*$CH_2$); 6.03 (*d*, *J* = 10.2, H–C(7)); 6.56 (*d*, *J* = 8.2, H–C(1)); 6.63 (*d*, *J* = 8.2, H–C(2)); 6.70 (*d*, *J* = 10.2, H–C(8)). $^{13}$C-NMR (101 MHz, $CDCl_3$): 17.50 (*q*); 17.97 (*q*); 21.25 (*t*); 25.85 (*t*); 26.05 (*q*); 35.09 (*t*); 42.85 (*q*, MeN); 44.41 (*s*); 45.85 (*t*); 47.26 (*s*); 56.36; 58.81; 92.85 (*s*, C(5)); 113.24 (*d*); 118.37 (*d*); 119.13 (*d*); 126.58 (*s*); 130.66 (*d*, C(7)); 132.87 (*s*); 135.66 (*s*); 141.96 (*s*); 143.85 (*s*); 156.24 (*d*, C(8)); 196.91 (*s*, C(6)). EI-MS: 379 (100). HR-EI-MS: 379.3147 ($C_{24}H_{29}NO_3^+$; calc. 379.2147).

*(5α,14β)-7,8-Didehydro-4,5-epoxy-14-(hexa-2,4-dienyl)-3-methoxy-5,17-dimethylmorphinan-6-one* (**10f**) *from* **8f**. Yield 43%. $R_f$ (AcOEt) 0.57. IR (film): 1679 (C=O). $^1$H-NMR (270 MHz, $CDCl_3$): 1.46 (*m*, 1 H); 1.70 (*s*, 3 H); 1.74 (*d*, *J* = 8.8, 3 H); 2.05 (*dd*, *J* = 12.2, 7.3, 1 H, MeCH=CHCH=CHC$H_2$); 2.19–2.33 (*m*, 3 H); 2.36 (*s*, MeN); 2.57 (*m*, 1 H); 3.09–3.14 (*m*, 2 H); 3.67 (*dd*, *J* = 12.3, 8.5, 1 H, MeCH=CHCH=CHC$H_2$); 3.79 (*s*, MeO–C(5)); 5.47 (*m*, MeCH=CHCH=C*H*$CH_2$); 5.64 (*m*, MeCH=C*H*CH=CHC$H_2$); 6.02–6.14 (*m*, H–C(7), MeC*H*=CHC*H*=CHC$H_2$); 6.56 (*d*, *J* = 8.3, H–C(1)); 6.62 (*d*, *J* = 8.3, H–C(2)); 6.66 (*dd*, *J* = 10.2, 3.4, H–C(8)). $^{13}$C-NMR (75 MHz, $CDCl_3$): 17.35 (*q*); 17.94 (*q*); 21.14 (*t*); 25.74 (*t*); 39.5 (*t*); 42.66 (*q*); 44.28 (*s*); 45.74 (*t*); 47.08 (*s*); 56.23 (*d*); 58.61 (*q*); 92.64 (*s*, C(5)); 113.11 (*d*, C(2)); 119.09 (*d*, C(1)); 124.78 (*d*, C(19)); 126.39 (*d*, MeCH=*C*HCH=CHCH$_2$); 128.41 (*d*); 130.74 (*d*); 131.09 (*d*); 132.59 (*s*); 134.54 (*d*); 141.84 (*s*); 143.71 (*s*); 155.61 (*d*, C(8)); 196.76 (*s*, C(6)). EI-MS: 391 (100, $M^+$), 244 (99), 243 (93). HR-EI-MS: 391.2148 ($C_{25}H_{29}NO_3^+$; calc. 391.2147).

*(5β,14β,18*E*)-7,8-Didehydro-4-hydroxy-3-methoxy-17-methyl-18-(3-phenylprop-2-enylidene)morphinan-6-one* (**11h**) *from* **7h**. Yield 71%. $R_f$ (AcOEt) 0.69. IR (film): 3340 (OH), 1678 (C=O). $^1$H-NMR (270 MHz, $CDCl_3$): 1.51 (*m*, 1 H); 1.92 (*m*, 1 H); 2.07 (*m*, 1 H); 2.35 (*m*, 1 H); 2.39 (*s*, MeN); 2.43 (*m*, 1 H); 2.73 (*dd*, *J* = 18.6, 5.8, 1 H); 3.15 (*m*, 1 H); 3.19 (*d*, *J* = 12.2, 1 H); 3.56 (*dd*, *J* = 16.7, 2.1, 1 H); 3.78 (*s*, MeO); 4.34

(*s*, H–C(5)); 5.71 (*dd*, *J* = 9.6, H–C(7)); 5.79 (*s*, OH–C(4)); 6.49 (*d*, *J* = 15.5, PhC*H*=CHCH); 6.55–6.64 (*m*, H–C(1), H–C(2), PhCH=CHC*H*); 6.76–6.88 (*m*, H–C(8), PhCH=C*H*CH); 7.14–7.40 (*m*, Ph). $^1$H,$^1$H-NOESY ($CDCl_3$; selected crosspeaks): 4.34 (*s*, H–C(5))/6.55–6.64 (H–C(1), H–C(2), PhCH=CHC*H*). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 24.79 (*t*); 30.82 (*t*); 32.82 (*t*); 43.12 (*q*, MeN); 45.85 (*t*, C(16)); 49.45 (*s*); 49.59 (*s*); 55.90 (*q*, MeO); 56.57 (*d*, C(10)); 67.41 (*d*, C(5)); 108.62 (*d*); 118.06 (*d*); 125.53 (*s*); 126.24 (*d*); 126.31 (*d*); 127.38 (*d*); 128.55 (*d*); 128.63 (*d*); 128.76 (*d*); 130.91 (*s*); 132.05 (*d*); 137.55 (*s*); 140.05 (*s*); 143.14 (*s*); 144.61 (*s*); 154.92 (*d*); 196.24 (*s*, C(6)). EI-MS: 439 (100, $M^+$). HR-EI-MS: 439.2155 ($C_{29}H_{29}NO_3^+$; calc. 439.2147).

*(5α,14β)-7,8-Didehydro-4,5-epoxy-3-methoxy-5,17-dimethyl-14-(3-phenylprop-2-enyl)morphinan-6-one* (**10a**) *from* **8a**. Yield 78%. $R_f$ (AcOEt) 0.64. IR (film): 1678 (C=O). $^1$H-NMR (270 MHz, $CDCl_3$): 1.51 (*m*, 1 H); 1.74 (*s*, 3 H); 2.16–2.38 (*m*, 3 H); 2.36 (*m*, 1 H,PhCH=CHC$H_2$); 2.40 (*s*, MeN); 2.62 (*m*, 1 H); 3.14 (*d*, *J* = 18.7, 1 H); 3.19 (*d*, *J* = 5.3, 1 H); 3.80 (*s*, MeO); 3.85 (*m*, 1 H, PhCH=CHC$H_2$); 6.09 (*d*, *J* = 10.1, H–C(7)); 6.17 (*m*, PhCH=C*H*CH$_2$); 6.51 (*d*, *J* = 15.8, PhC*H*=CCHCH$_2$); 6.56 (*d*, *J* = 8.3, H–C(1)); 6.63 (*d*, *J* = 8.3, H–C(2)); 6.71 (*d*, *J* = 10.1, H–C(8)); 7.20–7.37 (*m*, Ph). $^{13}$C-NMR (67.8 MHz, $CDCl_3$): 17.50 (*q*, *Me*–C(5)); 21.38 (*t*); 26.00 (*t*); 40.08 (*t*); 42.83 (*q*, MeN), 44.61 (*s*); 45.96 (*t*); 47.39 (s); 56.58; 58.99; 92.81 (*s*, C(5)); 113.76 (*d*, C(2)); 119.29 (*d*, C(1)); 124.34 (*d*); 126.12 (*d*); 126.55 (*s*); 127.42 (*d*); 128.61 (*d*); 131.13 (*d*); 132.79 (*s*); 134.24 (*d*); 137.22 (*s*); 142.11 (*s*); 144.03 (*s*); 155.32 (*d*, C(8); 196.88 (*s*, C(6)). EI-MS: 427 (100), 244 (58), 243 (82). HR-EI-MS: 427.2156 ($C_{28}H_{29}NO_3^+$; calc. 427.2147).

*(5α,14β)-4,5-Epoxy-3-methoxy-5,17-dimethyl-14-(3-phenylprop-2-enyl)morphinan-6-one* (**16a**) *from* **14a**. Yield 54%. $R_f$ ($CH_2Cl_2$/MeOH 90:10) 0.79. IR ($CHCl_3$): 1721 (C=O). $^1$H-NMR (300 MHz, C*D*$Cl_3$): 1.65 (*s*, Me–C(5)); 2.42 (*s*, MeN); 2.50 (*dd*, *J* = 8.2, 13.5, 1 H, PhCH=CHC$H_2$); 3.00 (*d*, *J* = 6.8, H–C(9)); 3.10 (*d*, *J* = 18.3, $H_b$–C(10)); 3.78 (*dd*, *J* = 7.6, 13.5, 1 H, PhCH=CHC$H_2$); 3.86 (*s*, MeO–C(3)); 6.25 (*m*, PhCH=C*H*CH$_2$); 6.55 (*d*, *J* = 15.4, PhC*H*=CHCH$_2$); 6.62 (*d*, *J* = 8.3, H–C(1)); 6.67 (*d*, *J* = 8.3, H–C(2)); 7.35 (*m*, Ph). $^{13}$C-NMR (75 MHz, $CDCl_3$): 17.5 (*Me*–C(5); 20.2; 25.9; 26.5; 31.6; 35.4; 41.1; 43.0; 46.0; 49.6; 56.4; 59.7; 95.3 (C(5)); 113.5; 119.1; 125.4; 126.0; 127.3; 128.6; 130.8; 133.3; 137.3; 142.5; 144.4; 212.0 (C(6)). EI-MS: 429 (100). HR-EI-MS: 429.2291 ($C_{28}H_{31}N_1O_3^+$; calc. 429.2303).

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