

Synthesis of 5-Methoxymethyl, 5-(2-Methoxyethyl), and 5-Allyl Thebaine, Codeinone, and Morphinone Derivatives*

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Abstract—Simple routes to 5-methoxymethylthebaine, 5-(2-methoxyethyl)thebaine, 5-allylthebaine, and similarly substituted codeinones and morphinones are described.

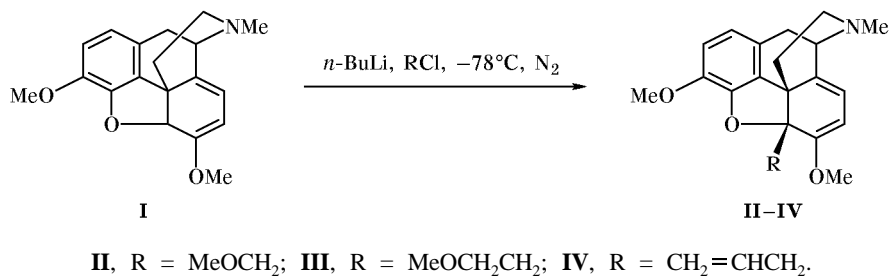
The goal of this work was to prepare a new series of 5-substituted thebaine derivatives and convert them into the corresponding codeinones and morphinones. It was expected that the resulting morphine-like and codeine-like compounds will show a reduced addiction effect while keeping their analgetic effect.

Metalation of thebaine (**I**) at the C⁵ atom was performed according to the known procedure [1], and subsequent alkylation gave substrates which were then converted into 5-substituted codeinone and morphinone derivatives. A solution of thebaine (**I**) in tetrahydrofuran was treated with 1.6 equiv of 2.5 M *n*-butyllithium in hexane. Quenching of the resulting solution with chloromethyl methyl ether afforded 5-methoxymethylthebaine (**II**) in 30% yield. Alkylation of the thebaine anion with 2-chloroethyl methyl ether gave 5-(2-methoxyethyl)thebaine (**III**) (57.4% on the reacted initial compound). 5-Allylthebaine (**IV**) was synthesized in 80% yield by treatment of a solution containing thebaine anion with allyl chloride

(Scheme 1). Our attempts to convert 5-substituted thebaines into 5-substituted codeinones with mercury acetate were unsuccessful. Therefore, the oxidation was carried out using peroxyformic acid on heating (Scheme 2). It is known that the oxidation of 5-benzylthebaine [2] with hydrogen peroxide in formic acid [3] in 65 h at 0°C leads to 5-benzyl-14-hydroxycodeinone (**V**) [2] in an improved yield (61%). By oxidation of 5-methoxymethylthebaine (**II**) with a mixture of formic acid and hydrogen peroxide at 4°C (70 h) we obtained 5-methoxymethyl-14-hydroxycodeinone (**VI**) in 62% yield. 5-(2-Methoxyethyl)-14-hydroxycodeinone (**VII**) and 5-allyl-14-hydroxycodeinone (**VIII**) were synthesized in 60 and 85% yield, respectively, by treatment of **III** and **IV** with hydrogen peroxide in formic acid at 4°C (66 h).

It should be noted that the presence of a hydroxy group in position 14 of the morphine skeleton was reported [4–6] to advantageously influence pharmacological properties.

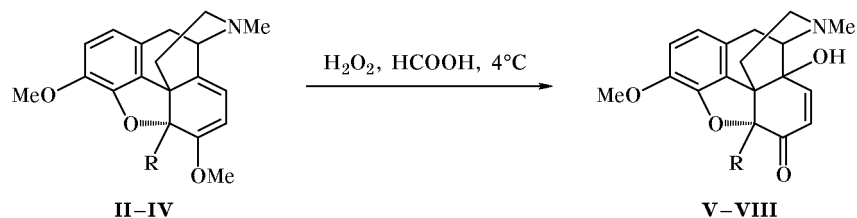
Scheme 1.



[†] Deceased.

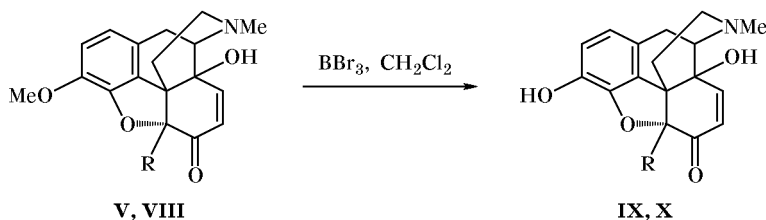
* The original article was submitted in English.

Scheme 2.



II, VI, R = MeOCH₂; III, VII, R = MeOCH₂CH₂; IV, VIII, R = CH₂=CHCH₂; V, R = PhCH₂ [2].

Scheme 3.



V, IX, R = PhCH₂; VIII, X, R = CH₂=CHCH₂.

A solution of 5-benzyl-14-hydroxycodeinone (V) in methylene chloride was treated with boron tribromide at -20°C over a period of 20 h. The reaction afforded 73% of 5-benzyl-14-hydroxymorphinone (IX) (Scheme 3). All attempts to convert in such a way compounds VI and VII into the corresponding morphinones failed: the reaction with BBr₃ resulted in loss of the methoxy group from the substituent on C⁵. Treatment of a solution of 5-allyl-14-hydroxycodeinone (VIII) with BBr₃ at room temperature (reaction time 20 h) gave 67.5% of 5-allyl-14-hydroxymorphinone (X) (Scheme 3).

Photochemical properties of the prepared codeinone and morphinone derivatives will be the subject of a separate communication.

EXPERIMENTAL

The ¹H NMR spectra were recorded on Varian EX-200 (200 MHz) and Unity 500 (500 MHz) spectrometers using chloroform-*d* as solvent and internal reference. The ¹³C NMR spectra were obtained with and without decoupling from protons on a Unity 500 instrument (500 MHz) using chloroform as solvent and internal reference. The IR spectra were measured on a Perkin-Elmer Model 298 or FTIR spectrometer. The chemical ionization mass spectra were obtained on a Hewlett-Packard 5987A GC-MS system using isobutene as chemical ionization gas. Elemental analysis was performed at Quantitative Technologies Inc. Laboratories, Whitehouse, NJ. The melting points

were determined on a Thomas Hoover capillary melting point apparatus; corrected values are given.

5-Methoxymethylthebaine (II). A solution of 5 g of thebaine in 250 ml of tetrahydrofuran was placed in a flame-dried round-bottom flask, and 9.64 ml (1.5 equiv) of a 2.5 M solution of *n*-butyllithium in hexane was added with stirring at -78°C under nitrogen. The mixture immediately turned deep wine-red. It was stirred for 20 min at -78°C , 1.83 ml of chloromethyl methyl ether was added, and the mixture was stirred for 20 min at -78°C , allowed to warm up to room temperature, and left overnight. The color changed to yellow. Distilled water, 5.0 ml, was added dropwise, and most part of the solvent was removed under reduced pressure. The brown residue was dissolved in chloroform, and the solution was washed with two portions of water, filtered through anhydrous magnesium sulfate, and concentrated. The residue was subjected to chromatography on silica gel using chloroform-methanol (2:1) as eluent. Yield 30%. Recrystallization from hexane gave green crystals with mp $126-128^{\circ}\text{C}$. ¹H NMR spectrum (CDCl₃), δ , ppm: 6.65 d (1H, $J = 8.3$ Hz), 6.59 d (1H, $J = 8.1$ Hz), 5.57 d (1H, $J = 6.6$ Hz), 5.19 d (1H, $J = 6.4$ Hz), 4.14 d (1H, $J = 9.2$ Hz), 3.82 s (3H, OMe), 3.82 d (1H, $J = 9.2$ Hz), 3.62 d (1H, $J = 5.4$ Hz), 3.59 s (3H), 3.36 s (3H, OMe), 3.25 d (1H, $J = 17.6$ Hz), 2.45–2.9 m (4H), 2.45 s (3H, NMe), 1.67 d.d (1H, $J = 2.2, 2.4$ Hz). IR spectrum (CDCl₃), ν , cm⁻¹: 2910, 2820, 2240, 1600, 1490, 1440, 1271, 1227, 1100, 1048, 905, 725. Mass spectrum (CI), m/z

(I_{rel} , %): 356 ($M^+ + 1$, 100), 355 (23), 324 (4), 310 (2). Found, %: C 71.37; H 7.10; N 3.95. $\text{C}_{21}\text{H}_{25}\text{NO}_4$. Calculated, %: C 70.98; H 7.04; N 3.94. M 355.

5-(2-Methoxyethyl)thebaine (III). A 2.5 M solution of *n*-butyllithium in hexane, 10 ml, was added with stirring at -78°C under nitrogen to a solution of 5.00 g of thebaine in 250 ml of tetrahydrofuran (freshly distilled over sodium diphenylketyl). The mixture immediately turned deep wine-red. It was stirred for 25 min at -78°C , 2.2 ml (1.5 equiv) of freshly distilled 2-chloroethyl methyl ether was added, and the mixture was stirred for 30 min at -78°C , allowed to warm up to room temperature, and left overnight. The color changed to orange-yellow. Water, 5.00 ml, was added, and most part of the solvent was removed under reduced pressure. The yellow-brown residue was dissolved in methylene chloride, and the solution was washed with two portions of water, filtered through anhydrous magnesium sulfate, and concentrated. The residue was subjected to chromatography on silica gel using $\text{MeOH}-\text{CH}_2\text{Cl}_2$ (1:9) as eluent to isolate 2.01 g of compound **III** as a pale yellow oil (57.4%, calculated on the reacted thebaine) and 1.5 g of the initial compound. ^1H NMR spectrum (CDCl_3 , 500 MHz), δ , ppm: 1.69 d.d (1H, $J = 2.4, 2.2$ Hz), 2.23–2.35 m (3H), 2.46 s (3H, NMe), 2.62–2.80 m (4H), 3.28 d (1H, $J = 17.6$ Hz), 3.31 s (3H, OMe), 3.46 m (1H), 3.56 s (3H, OMe), 3.64 d (1H, $J = 6.6$ Hz), 3.83 s (3H, OMe), 5.04 d (1H, $J = 6.5$ Hz), 5.55 d (1H, $J = 6.4$ Hz), 6.58 d (1H, $J = 8.1$ Hz), 6.63 d (1H, $J = 8.3$). ^{13}C NMR spectrum (CDCl_3 , 500 MHz), δ_{C} , ppm: 154.48, 143.45, 142.59, 134.63, 132.30, 127.13, 119.38, 112.60, 112.30, 96.53, 94.47, 68.81, 61.65, 58.86, 56.23, 54.99, 47.42, 45.82, 42.48, 33.06, 30.59, 29.86. IR spectrum (CDCl_3), ν , cm^{-1} : 2920, 1600, 1495, 1440, 1278, 1250, 1230, 1100, 1049, 1010, 905. Mass spectrum (CI), m/z (I_{rel} , %): 370 ($M^+ + 1$, 100), 368 (4), 312 (7), 310 (2). Found, %: C 71.59; H 7.38; N 3.76. $\text{C}_{22}\text{H}_{27}\text{NO}_4$. Calculated, %: C 71.54; H 7.32; N 3.79. M 369.

5-Allylthebaine (IV). A 2.5 M solution of *n*-butyllithium in hexane, 10 ml, was added with stirring at -78°C under nitrogen to a solution of 5.00 g of thebaine in 300 ml of tetrahydrofuran (freshly distilled over sodium diphenylketyl). The mixture immediately turned deep wine-red. The mixture was stirred for 30 min at -78°C , 2 ml of freshly distilled allyl chloride was added, and the mixture was stirred for 30 min at -78°C , allowed to warm up to room temperature, and left overnight. The color changed to yellow. Water, 5 ml, was added, and most part of the solvent was removed under reduced pressure. The

yellow-brown residue was dissolved in chloroform, and the solution was washed with two portions of water, filtered through anhydrous magnesium sulfate, and concentrated. The residue was subjected to chromatography on silica gel using methanol-chloroform (1:9) as eluent. Yield 4.00 g (80%). The product was recrystallized from hexane. Yellow-brown crystals, mp $104-105^\circ\text{C}$. ^1H NMR spectrum (CDCl_3), δ , ppm: 6.63 d (1H, $J = 8.3$ Hz), 6.55 d (1H, $J = 8$ Hz), 5.7 m (1H), 5.53 d (1H, $J = 6.6$ Hz), 5.16 m (3H), 3.85 d (1H, $J = 5.8$ Hz), 3.85 s (3H), 3.62 d (1H, $J = 8$ Hz), 3.56 s (3H), 3.24 m (2H), 2.57–2.93 m (4H), 2.45 s (3H), 1.68 d.d (1H, $J = 2.2, 2.4$ Hz). ^{13}C NMR spectrum (CDCl_3 , 500 MHz), δ_{C} , ppm: 154.18, 151.15, 143.41, 142.38, 134.66, 132.85, 132.05, 127.05, 119.18, 118.16, 112.30, 112.12, 95.31, 61.45, 56.07, 54.87, 47.25, 45.66, 42.36, 37.36, 30.34, 59.54. IR spectrum (CDCl_3), ν , cm^{-1} : 2920, 2220, 1598, 1493, 1435, 1271, 1220, 1100, 1049, 902. Mass spectrum (CI), m/z (I_{rel} , %): 352 ($M^+ + 1$, 100), 336 (2), 310 (1), 295 (2), 216 (1). Found, %: C 75.28; H 7.23; N 3.95. $\text{C}_{22}\text{H}_{25}\text{NO}_3$. Calculated, %: C 75.21; H 7.12; N 3.98. M 351.

5-Benzyl-14-hydroxycodeinone (V). An ice-cold mixture of 1.2 ml of 0.7% H_2SO_4 , 0.35 ml of 88% HCO_2H , and 0.7 ml of 30% H_2O_2 was added to 1.00 g (2.49 mmol) of 5-benzylthebaine. The mixture was stirred at 0°C until it became transparent (~ 30 min). The resulting solution was kept for 65 h in a refrigerator (4°C) and poured into 20 ml of ice water which was made alkaline by addition of a concentrated ammonia solution. The mixture was extracted with 5 portions of chloroform, and the organic extracts were combined, dried over magnesium sulfate, and evaporated to obtain 0.61 g (61%) of 5-benzyl-14-hydroxycodeinone (**V**). Recrystallization from hexane gave off-white needles with mp $177-178^\circ\text{C}$. ^1H NMR spectrum (CDCl_3 , 500 MHz), δ , ppm: 1.48 d.d (1H, $J = 3.6, 3.5$ Hz), 2.2 d.d.d (1H, $J = 3.6, 3.9$ Hz), 2.46 s (3H), 2.46 m (3H), 2.92 d (1H, $J = 5.4$ Hz), 3.17 d (1H, $J = 18.3$ Hz), 3.38 d (1H, $J = 14.6$ Hz), 3.6 d (1H, $J = 14.6$ Hz), 3.85 s (3H), 4.8 br.s (1H), 6.08 d (1H, $J = 10$ Hz), 6.51 d (1H, $J = 10$ Hz), 6.57 d (1H, $J = 8.3$ Hz), 6.65 d (1H, $J = 8.3$ Hz), 7.26 m (5H). ^{13}C NMR spectrum (CDCl_3 , 500 MHz), δ_{C} , ppm: 198.12, 146, 143.56, 142.6, 135.24, 133.56, 131.42, 130.73, 127.85, 126.59, 124.64, 119.09, 114.72, 94.53, 68.16, 64.49, 56.71, 48.4, 45.35, 42.37, 37.46, 26.4, 22.44. IR spectrum (CHCl_3), ν , cm^{-1} : 3330, 1670. Mass spectrum (CI), m/z (I_{rel} , %): 404 ($M^+ + 1$, 100), 386 (1), 319 (1), 298 (6). Found, %: C 74.37; H 6.34; N 3.41. $\text{C}_{23}\text{H}_{25}\text{NO}_4$. Calculated, %: C 74.44; H 6.2; N 3.47. M 403.

14-Hydroxy-5-methoxymethylcodeinone (VI).

An ice-cold mixture of 0.65 ml of 0.7% H₂SO₄, 0.2 ml of 88% HCO₂H, and 0.4 ml of 30% H₂O₂ was added to 0.5 g (1.4 mmol) of 5-methoxymethylthebaine. The mixture was stirred at 0°C until it became homogeneous (~25 min), kept for 70 h in a refrigerator (4°C), and poured into 5 ml of ice water which was made alkaline by addition of a concentrated ammonia solution. The mixture was extracted with 5 portions of chloroform, and the extracts were combined, dried over magnesium sulfate, and evaporated to obtain 0.31 g (62%) of 14-hydroxy-5-methoxymethylcodeinone (VI). Recrystallization from chloroform-hexane (1:20) gave off-white crystals, mp 145–147°C. ¹H NMR spectrum (CDCl₃, 500 MHz), δ, ppm: 1.56 d.d (1H, *J* = 2.2, 2.4 Hz), 2.2–2.4 m (4H), 2.44 s (3H, NMe), 3.15 d (1H, *J* = 5.2 Hz), 3.25 d (1H, *J* = 18.6 Hz), 3.42 s (3H, OMe), 3.81 s (3H, 3-OMe), 3.94 d (1H, *J* = 8.5 Hz), 4.12 d (1H, *J* = 8.5 Hz), 4.3 br.s (1H), 6.07 d (1H, *J* = 10.2 Hz), 6.65 m (3H). ¹³C NMR spectrum (CDCl₃, 500 MHz), δ_C, ppm: 196.85, 148.98, 142.98, 142.65, 132.22, 131.46, 125.53, 119.73, 114.14, 90.79, 70.12, 67.92, 62.84, 59.89, 56.45, 48.32, 45.76, 42.57, 25.32, 22.27. IR spectrum (CHCl₃), ν, cm⁻¹: 3410, 1670. Mass spectrum (CI), *m/z* (*I*_{rel}, %): 358 (*M*⁺ + 1, 100), 328 (4), 314 (30). Found, %: C 67.22; H 6.50; N 3.89. C₂₀H₂₃NO₅. Calculated, %: C 67.22; H 6.44; N 3.92.

14-Hydroxy-5-(2-methoxyethyl)codeinone (VII).

An ice-cold mixture of 1.6 ml of 0.7% H₂SO₄, 0.50 ml of 88% HCO₂H, and 1.0 ml of 30% H₂O₂ was added to 1.3 g (3.5 mmol) of 5-(2-methoxyethyl)thebaine. The mixture was stirred at 0°C until it became homogeneous (~15 min), kept for 60 h in a refrigerator (4°C), and poured into 20 ml of ice water which was made alkaline (pH 9) by addition of a concentrated ammonia solution. It was then extracted with several portions of methylene chloride, the extracts were combined and dried over MgSO₄, and the solvent was removed to obtain 0.78 g (60%) of 14-hydroxy-5-(2-methoxyethyl)codeinone (VII) as a pale green oil. ¹H NMR spectrum (CDCl₃, 500 MHz), δ, ppm: 1.51 d.d (1H, *J* = 2.4, 2.2 Hz), 2.17–2.42 m (3H), 2.44 s (3H, NMe), 2.47–2.69 m (3H), 3.00 d (1H, *J* = 5.6 Hz), 3.2 d (1H, *J* = 18.6 Hz), 3.26 s (3H, OMe), 3.65 m (1H), 3.79 m (1H), 3.82 s (3H, OMe), 5.2 br.s (1H), 6.12 d (1H, *J* = 10 Hz), 6.53 d (1H, *J* = 10.2 Hz), 6.59 d (1H, *J* = 8.3 Hz), 6.65 d (1H, *J* = 8 Hz). IR spectrum (CDCl₃), ν, cm⁻¹: 3340, 1678. Mass spectrum (CI), *m/z* (*I*_{rel}, %): 372 (*M*⁺ + 1, 100), 356 (4), 340 (5), 314 (22). Found, %: C 67.96; H 6.79; N 3.78. C₂₁H₂₅NO₅. Calculated, %: C 67.92; H 6.74; N 3.77. *M* 371.

5-Allyl-14-hydroxycodeinone (VIII). An ice-cold mixture of 1.3 ml of 0.7% H₂SO₄, 0.4 ml of 88% HCO₂H, and 0.8 ml of 30% H₂O₂ was added to 1 g (2.8 mmol) of 5-allylthebaine, and the mixture was stirred at 0°C until it became homogeneous (20 min), kept for 66 h in a refrigerator (4°C), and poured into 20 ml of ice water which was made alkaline (pH 9) by addition of a concentrated ammonia solution. The mixture was extracted with several portions of chloroform, and the organic extracts were combined, dried over magnesium sulfate, and evaporated to isolate compound VIII in 85% yield. Recrystallization from hexane gave bright yellow needles with mp 147–149°C. ¹H NMR spectrum (CDCl₃), δ, ppm: 1.54 d.d (1H, *J* = 2.2, 2.4 Hz), 2.32 d.d.d (1H, *J* = 3.53, 3.48, 3.61 Hz), 2.42–2.56 m (3H), 2.45 s (3H, NMe), 2.82 d.d (1H, *J* = 6.68, 6.63 Hz), 3.04 d (1H, *J* = 8.06 Hz), 3.15 d.d (1H, *J* = 6.7, 6.68 Hz), 3.22 d (1H, *J* = 18.3 Hz), 3.82 s (3H, 3-OMe), 5.11 m (3H), 6.11 d (1H, *J* = 10 Hz), 6.11 m (1H), 6.54 d (1H, *J* = 9.89 Hz), 6.62 d (1H, *J* = 8.18 Hz), 6.67 d (1H, *J* = 8.2 Hz). ¹³C NMR spectrum (CDCl₃, 500 MHz), δ_C, ppm: 197.85, 146.25, 143.57, 142.53, 134.23, 131.75, 131.48, 124.76, 119.11, 118.59, 114.16, 94.01, 68.02, 64.63, 56.48, 47.99, 45.27, 42.43, 35.88, 26.27, 22.37. IR spectrum (CHCl₃), ν, cm⁻¹: 3330, 1673. Mass spectrum (CI), *m/z* (*I*_{rel}, %): 354 (*M*⁺ + 1, 100), 336 (6), 314 (3), 269 (2), 217 (3). Found, %: C 71.13; H 6.62; N 3.96. C₂₁H₂₃NO₄. Calculated, %: C 71.38; H 6.51; N 3.96. *M* 353.

5-Benzyl-14-hydroxymorphinone (IX). A 25-ml flame-dried round-bottom flask was charged with 20 mg (0.049 mmol) of 5-benzylcodeinone and 3 ml of freshly distilled methylene chloride (preliminarily dried over calcium hydride). The solution was cooled in a cryogenic bath to –12°C under nitrogen, 0.04 ml (0.42 mmol) of boron tribromide was added, and the mixture was stirred for 20 h at –12°C. Methanol, 0.5 ml, was then added, and the mixture was treated with a saturated solution of NaHCO₃ and extracted with methylene chloride. The aqueous layer was thoroughly extracted with a mixture of methylene chloride with ethanol (3:2), and the extracts were combined, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was 5-benzylmorphinone hydrobromide. It was dissolved in methanol, and the solution was treated with a solution of NaHCO₃. The free base was extracted into methylene chloride, the extract was dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure to obtain 14.6 mg (73%) of compound IX as a green foam-like material. ¹H NMR spectrum, δ, ppm: 1.50 d.d (1H, *J* = 3.7,

3.5 Hz), 2.25 m (1H), 2.44 s (3H, NMe), 2.5 m (3H), 2.96 d (1H, $J = 4.7$ Hz), 3.18 d (1H, $J = 18.5$ Hz), 3.35 d (1H, $J = 14.9$ Hz), 3.56 d (1H, $J = 14.6$ Hz), 5.2 br.s (2H), 6.08 d (1H, $J = 10.3$ Hz), 6.55 m (2H), 6.66 d (1H, $J = 8.3$ Hz), 7.28 m (5H). IR spectrum (CHCl_3), ν , cm^{-1} : 3320 br, 1675. Mass spectrum (CI), m/z (I_{rel} , %): 390 ($M^+ + 1$, 100), 372 (6), 351 (5), 300 (2). Found, %: C 73.96; H 5.97; N 3.56. $\text{C}_{24}\text{H}_{23}\text{NO}_4$. Calculated, %: C 74.04; H 5.91; N 3.60. M 389.

5-Allyl-14-hydroxymorphinone (X). A solution of 200 mg (0.567 mmol) of 5-allyl-14-hydroxycodone in 2 ml of methylene chloride was added to a 1 M solution of boron tribromide in methylene chloride (1.1 ml, 11.6 mmol). The mixture was stirred for 20 h at room temperature and poured into 20 ml of an ice-cold dilute ammonia solution. The resulting mixture was stirred for 30 min at 0°C . The aqueous layer was separated, and the organic phase was extracted with 10 ml of a 1 M solution of sodium hydroxide. The aqueous layers were combined and adjusted to pH 9.5 by adding a solution of NaOH. The solution was then saturated with sodium chloride and extracted with several portions of methylene chloride. The organic extracts were combined and dried over magnesium sulfate, and the solvent was removed under reduced pressure to isolate 135 mg (67.5%) of a yellow oil which showed in the ^1H NMR spectrum no characteristic methoxy group proton signal at δ 3.82 ppm. During drying some yellow crystals formed spontaneously. mp $199\text{--}201^\circ\text{C}$. ^1H NMR spectrum (CDCl_3 , 500 MHz), δ , ppm: 1.54 d.d (1H, $J = 2.7, 2.7$ Hz), 2.27 d.d.d (1H, $J = 3.7, 3.6, 3.6$ Hz), 2.41–2.57 m

(3H), 2.44 s (3H, NMe), 2.83 d.d (1H, $J = 6.4, 6.4$ Hz), 3.01 m (2H), 3.19 d (1H, $J = 18.6$ Hz), 5.11–5.15 m (2H), 6.05–6.15 m (1H), 6.11 d (1H, $J = 9.8$ Hz), 6.57 m (2H), 6.67 d (1H, $J = 8.3$ Hz). ^{13}C NMR spectrum (CDCl_3 , 500 MHz), δ_{C} , ppm: 198.70 (C=O), 146.97, 142.02, 138.57, 133.83, 131.55, 130.88, 124.09, 119.70, 118.87, 117.64, 94.44, 68.16, 64.64, 48.23, 45.30, 42.46, 35.89, 26.22, 22.43. IR spectrum (CHCl_3), ν , cm^{-1} : 3340 br, 1672. Mass spectrum (CI), m/z (I_{rel} , %): 340 ($M^+ + 1$, 100), 322 (2), 299 (2), 250 (1). Found, %: C 70.86; H 6.15; N 4.19. $\text{C}_{20}\text{H}_{21}\text{NO}_4$. Calculated, %: C 70.79; H 6.19; N 4.13.

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REFERENCES

1. Boden, R.M., Gates, M., Ho, S.P., and Sundararaman, P., *J. Org. Chem.*, 1982, vol. 47, p. 1347.
2. Gates, M., Boden, R.M., and Sundararaman, P., *J. Org. Chem.*, 1989, vol. 54, p. 972.
3. Schmidhammer, H., Deeter, J.B., Jones, N.D., Leander, J.D., Schoepp, D.P., and Swartzendruber, J.K., *Helv. Chim. Acta*, 1988, vol. 71, p. 1801.
4. Hosztafi, S., Simon, C., and Makleit, S., *Synth. Commun.*, 1992, vol. 22, p. 2527.
5. Casy, A.F. and Porfitt, R.T., *Opioid Analgesics. Chemistry and Receptors*, New York: Plenum, 1986, p. 414.
6. Ninan, A. and Sainsbury, M., *Tetrahedron*, 1992, vol. 48, p. 6709.