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Photochemistry of Some Codeinones and Morphinones*

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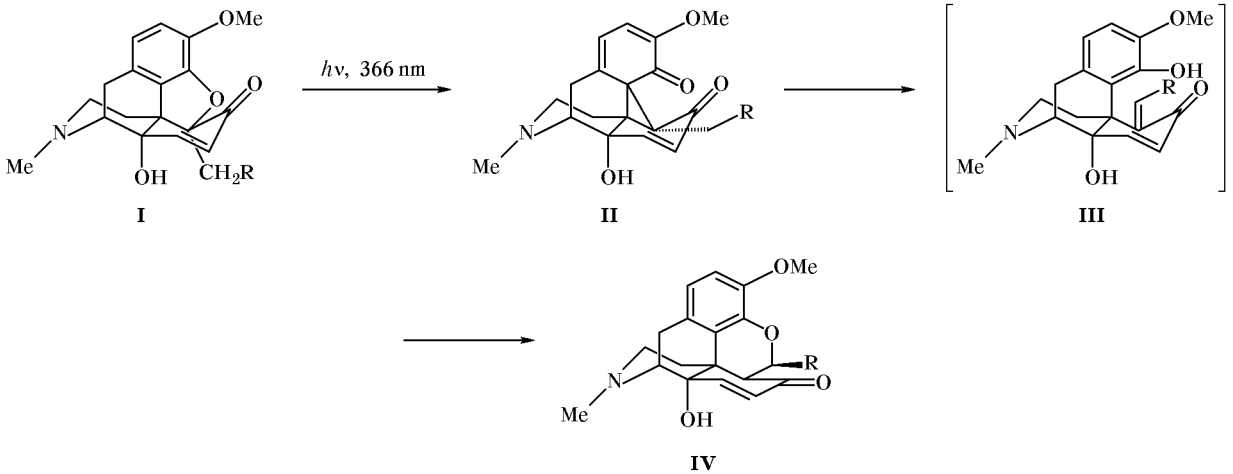
Abstract—Irradiation of 5-benzyl-, 5-methoxymethyl-, and 5-allyl-substituted codeinones and morphinones with UV light (λ 366 nm) leads to formation of the corresponding 18β-phenyl, 18β-methoxy, and 18β-vinyl derivatives of 4,5α-epoxymethanomorphin-7-en-6-one.

Schultz *et al.* previously reported [1] on the photochemistry of codeinone derivatives, which involved unique photoreactivity of the dihydrobenzofuran ring system [2–4]. The photorearrangements were initiated by UV irradiation at λ 366 nm [5]. In the present work we tried to extend analogous transformations to some other 5-substituted derivatives.

Irradiation of a solution of of 5-benzyl-14-hydroxycodeinone (**I**) [6] in methanol at λ 366 nm for 75 min, followed by chromatography on a silica gel plate, gave a colorless product together with the unreacted initial compound. By recrystallization from hexane we isolated benzopyran derivative **IV** as colorless crystals (yield 85%, calculated on the reacted **I**).

A plausible mechanism [1] of the photochemical rearrangement of 5-benzyl-14-hydroxycodeinone (**I**) into benzopyran (**IV**) includes isomerization of the initial compound into cyclopropane-spiro-2,4-cyclohexadienone **II** (Scheme 1). The latter undergoes unusual Claisen rearrangement (C→O migration of hydrogen) involving the 5-benzyl substituent to give intermediate dienone **III** which was not detected in the reaction mixture. Intramolecular Michael addition in **III** converts it to benzopyran **IV**. The formation

Scheme 1.



I **II** **III** **IV**

I–**IV**, R = Ph.

† Deceased.

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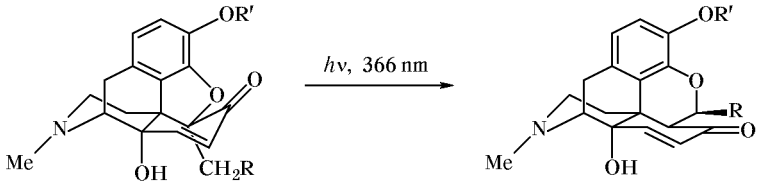
Scheme 2.



V, VII, IX, XI **VI, VIII, X, XII**

V, **VI**, R = MeO; **VII**, **VIII**, **XI**, **XII**, R = CH_2=CH; **IX**, **X**, R = Ph; **V**–**VIII**, R′ = Me; **IX**–**XII**, R′ = H.

of product **IV** is the first demonstration that the photorearrangement reported for 5-methylcodeinone [1] can be extended to include other C^5-substituted codeinone derivatives.

Irradiation of 5-methoxymethylcodeinone (**V**) in methanol at λ 366 nm for 3 h (further irradiation resulted in decomposition) and subsequent chromatographic separation afforded 25% of benzopyran **VI** as a brown oil (Scheme 2). Compound **VIII** was obtained by irradiation of a methanolic solution of 5-allyl-14-hydroxycodeinone (**VII**) at λ 366 nm over a period of 6 h. The yield of **VIII** was 60% (calculated on the reacted initial compound). Likewise, 5-benzyl-14-hydroxymorphinone (**IX**) and 5-allyl-14-hydroxymorphinone (**XI**) were converted into benzopyran derivatives **X** (yield 72%) and **XII** (51%), respectively, by irradiation at λ 366 nm for 2 and 6 h.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on Varian EX-200 (200 MHz) and Unity 500 (500 MHz) spectrometers using chloroform-*d* or benzene-d_6 as solvent and internal reference. The ^{13}C NMR spectra were obtained on a Varian Unity 500 instrument in chloroform. The IR spectra were measured on Perkin–Elmer Model 298 and FTIR spectrometers. The chemical ionization mass spectra were run on a Hewlett–Packard 5987A GC–MS system with the use of isobutene as chemical ionization gas.

General procedure for photochemical reactions. Appropriate substrate was dissolved in a spectrophotometric grade solvent to a required concentration (see below), and the solution was placed in a 5- or 30-ml test tube. The solution was irradiated with a Hanovia medium-pressure mercury arc lamp (450 W), which was placed in a uranyl glass sleeve (λ 366 nm) cooled with water. The entire apparatus and the sample were immersed in a water-cooled bath, and the sample was irradiated for a time indicated below. The solvent was removed under reduced pressure to afford the crude product.

14-Hydroxy-3-methoxy-17-methyl-18β-phenyl-4,5α-epoxymethanomorphin-7-en-6-one (IV). A solution of 0.012 g (0.030 mmol) of 5-benzyl-14-hydroxycodeinone in 5 ml of methanol was itrradiated at λ 366 nm over a period of 75 min. Removal of the solvent left a brown gum which was subjected to thin-layer chromatography on silica gel using chloroform–methanol (9:1) as eluent to isolate a colorless product and 0.006 g of the starting material. The product was recrystallized from hexane. Yield 0.0051 g (85% on the reacted initial compound). Colorless crystals with mp 180–182°C. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz), δ, ppm: 1.91 d.d (1H, *J* = 3.6, 3.5 Hz), 2.44 m (2H), 2.48 s (3H, NMe), 2.61 d (1H, *J* = 6.6 Hz), 2.72 d.d (1H, *J* = 12, 11 Hz), 2.97 d (1H, *J* = 6.1 Hz), 3.29 d (1H, *J* = 18.6 Hz), 3.55 d (1H, *J* = 2.4 Hz), 3.84 s (3H, 3-OMe), 4.8 br.s (1H), 5.68 d (1H, *J* = 1.9 Hz), 5.71 d (1H, *J* = 9.8 Hz), 6.43 d (1H, *J* = 10 Hz), 6.61 d (1H, *J* = 8.3 Hz), 6.72 d (1H, *J* = 8.3 Hz), 7.26 m (1H), 7.40 t (2H, *J* = 8.1, 7.5 Hz), 7.59 d (2H, *J* = 7.5 Hz). ^{13}C NMR spectrum ($CDCl_3$, 500 MHz), δ_C, ppm: 194.16, 146.87, 144.67, 140.88, 132.11, 127.88, 126.48, 124.81, 122.08, 118.14, 111.16, 72.35, 67.43, 61.67, 56.27, 48.19, 45.28, 42.41, 38.96, 34.15, 23.79. IR spectrum ($CHCl_3$), ν, cm^{-1}: 3500, 1700. Mass spectrum, *m*/*z* (I_{rel}, %): 404 (M^+ + 1, 100), 388 (10), 373 (2), 298 (12).

14-Hydroxy-3,18β-dimethoxy-17-methyl-4,5α-epoxymethanomorphin-7-en-6-one (VI). A solution of 20 mg (0.056 mmol) of 14-hydroxy-5-methoxymethylcodeinone in methanol (6 ml) was irradiated at λ 366 nm over a period of 3 h. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using chloroform–methanol (9:1) as eluent to isolate 5 mg (25%) of the product as a brown oil. ^{1}H NMR spectrum ($CDCl_3$, 200 MHz), δ, ppm: 1.55 br.s (1H), 2.2–2.7 m (4H), 2.4 s (3H, NMe), 2.91 d (1H, *J* = 4 Hz), 3.25 m (2H), 3.61 s (3H, OMe), 3.8 s (3H, OMe), 3.8 d (1H, *J* = 3.8 Hz), 5.97 d (1H, *J* = 10.09 Hz), 6.03 d (1H, *J* = 1.92 Hz), 6.6 m (3H). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1675, 3380. Mass spectrum, *m*/*z*

(I_{rel}, %): 358 (M^+ + 1, 45), 326 (100), 324 (10), 310 (12).

14-Hydroxy-3-methoxy-17-methyl-18β-vinyl-4,5α-epoxymethanomorphin-7-en-6-one (VIII). A solution of 20 mg (0.057 mmol) of 5-allyl-14-hydroxycodeinone in 6 ml of methanol was irradiated at λ 366 nm over a period of 6 h. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using chloroform–methanol (10 : 1) as eluent to isolate 10 mg of the initial compound and 6 mg (60% on the reacted starting material) of product **VIII** as a yellow oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.73 d.d (1H, *J* = 3.6, 1.8 Hz), 2.3 m (1H), 2.38 s (3H, NMe), 2.5–3.0 m (3H), 3.05 d (1H, *J* = 2 Hz), 3.2 d (1H, *J* = 20 Hz), 3.7 s (3H, OMe), 3.75 s (1H), 4.95 d (1H, *J* = 4 Hz), 5.24 m (2H), 5.8 d (1H, *J* = 10 Hz), 6.4 d (1H, *J* = 10 Hz), 6.55 d.d (2H, *J* = 8.8 Hz), 6.8 m (1H). IR spectrum ($CHCl_3$), ν, cm^{-1}: 3385, 1680. Mass spectrum, *m*/*z* (I_{rel}, %): 354 (M^+ + 1, 100), 338 (7), 311 (8), 276 (15).

3,14-Dihydroxy-17-methyl-18β-phenyl-4,5α-epoxymethanomorphin-7-en-6-one (X). A solution of 0.012 g (0.031 mmol) of 5-benzyl-14-hydroxymorphin-6-one (**IX**) in 6 ml of methanol was irradiated at λ 366 nm over a period of 2 h. The solvent was removed to obtain a brown gum which was subjected to chromatography on a silica gel plate using methylene chloride–methanol (9 : 1) as eluent. We isolated 0.003 g of the unreacted starting material and 0.0065 g (72% on the reacted initial compound) of product **X** as a pink foam. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz), δ, ppm: 1.9 m (1H), 2.5 m (1H), 2.49 s (3H, NMe), 2.3–2.6 m (3H), 2.97 d (1H, *J* = 5.6 Hz), 3.28 d (1H, *J* = 18.6 Hz), 3.52 d (1H, *J* = 2.2 Hz), 5.68 s (1H), 5.73 d (1H, *J* = 9.8 Hz), 6.45 d (1H, *J* = 10 Hz), 6.6 m (2H), 7.27–7.52 m (5H). IR spectrum ($CHCl_3$), ν, cm^{-1}: 3350 br, 1680. Mass spectrum, *m*/*z* (I_{rel}, %): 390 (M^+ + 1, 40), 313 (16), 270 (21), 254 (100).

3,14-Dihydroxy-17-methyl-18β-vinyl-4,5α-epoxymethanomorphin-7-en-6-one (XII). A solution of 10 mg (0.029 mmol) of 5-allyl-14-hydroxymorphin-6-one (**XI**) in 6 ml of methanol was irradiated at λ 366 nm over a period of 6 h. The solvent was removed to afford a brown residue which was subjected to chromatography on a silica gel plate using methylene chloride–methanol (9 : 1) to isolate 0.004 g of the unreacted initial compound and 0.0031 g (51% on the reacted **XI**) of compound **XII** as a pale yellow oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.73 m (1H), 2.3–2.9 m (4H), 2.38 s (3H, NMe), 3.05 d (1H, *J* = 2 Hz), 3.2 d (1H), *J* = 20 Hz), 3.75 s (1H), 5.0 d (1H, *J* = 4 Hz), 5.3 m (2H), 5.8 d (1H, *J* = 10 Hz), 6.4 d (1H, *J* = 10 Hz), 6.5–6.9 m (3H). IR spectrum ($CDCl_3$), ν, cm^{-1}: 3350 br, 1680.

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