

Synthesis of π -Complexes of Codeine with Iron and Molybdenum

Valery N. Kalinin,^{*a} Vladimir V. Derunov,^a Leendert Maat,^b Jin K. Park^c and Helmut Schmidhammer^d

^a A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 117813 Moscow, Russian Federation. Fax: +7 095 135 5085

^b Laboratory of Organic Chemistry and Catalysis, Delft University of Technology, Julianalaan 136, 2628 BL Delft, The Netherlands. Fax: +31 15 78 4700

^c Dong Kook Pharmaceutical Co., Ltd., Dae Chi-3 Dong, Kang Nam-Ku, 997-8 Seoul, Korea. Fax: +82 2 566 8542

^d Institute of Pharmaceutical Chemistry, University of Innsbruck, Innrain 52a, A-6020 Innsbruck, Austria. Fax: +43 512 507 2940

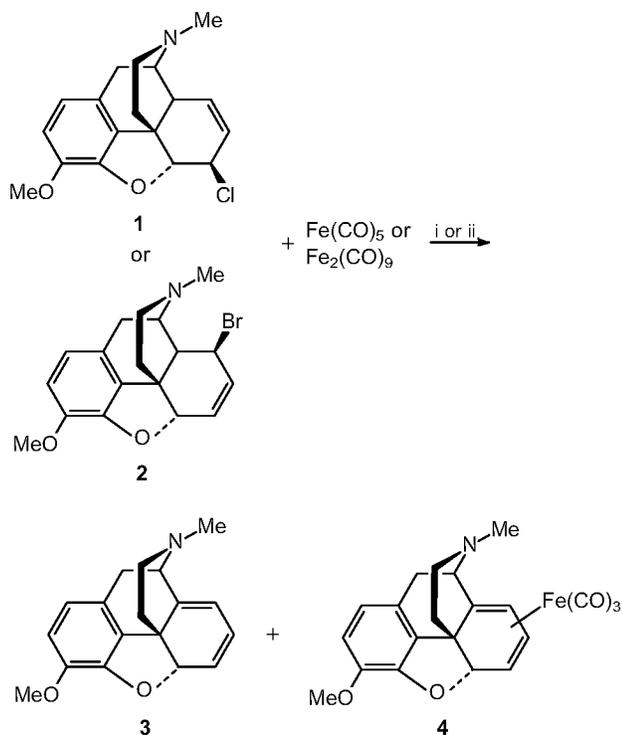
Treatment of 6 β -chloro-6-deoxycodeine **1** or 8 β -bromo-8-deoxypseudoecodeine **2** with Fe(CO)₅ or Fe₂(CO)₉ yields 6-demethoxythebaine **3** and the π -diene iron complex **4**; compound **1** or **2** reacts with Mo(CO)₆ to give the π -allylic molybdenum complexes **5** and **6**, respectively.

Reactions of transition metal complexes with morphine alkaloids are useful for the stereocontrolled introduction of substituents into the morphinan skeleton and for the protection of double bonds of ring C from destruction.¹

At present, complexes of iron^{2,3} and palladium⁴ with morphine alkaloids are known.

The wide variety of functionalisation in ring C of morphine alkaloids promotes preparation of various kinds of transition metal complexes.

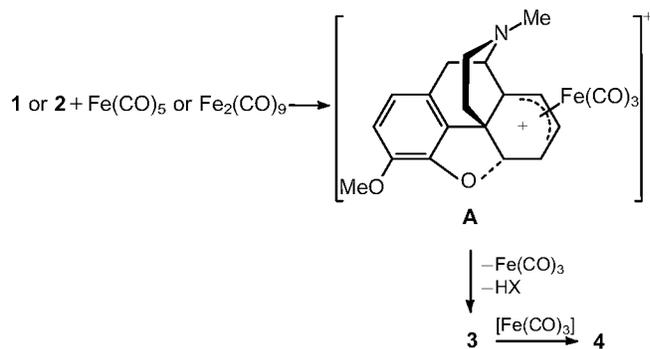
We have found that 6 β -chloro-6-deoxycodeine **1** or 8 β -bromo-8-deoxypseudoecodeine **2** reacts with an equimolar amount of Fe(CO)₅ or Fe₂(CO)₉ to give two products: 6-demethoxythebaine **3**^{5,6} and π -diene complex **4** (Scheme 1).



Scheme 1 Reagents and conditions: i, Fe(CO)₅, THF, 20 °C, *h* ν , 1 h; **3**: yield 35%; **4**: yield 40% (from **1**); **3**: yield 38%; **4**: yield 42% (from **2**); ii, Fe₂(CO)₉, benzene, 80 °C, 2 h; **3**: yield 15%; **4**: yield 48% (from **1**); **3**: yield 20%; **4**: yield 55% (from **2**).

The relation of yields of **3** and **4** depends on the amount of Fe(CO)₅ or Fe₂(CO)₉. Increasing the amount of Fe(CO)₅ or Fe₂(CO)₉ leads to an increase of the amount of **4**, and with a large excess of Fe(CO)₅ or Fe₂(CO)₉ **4** was formed exclusively.

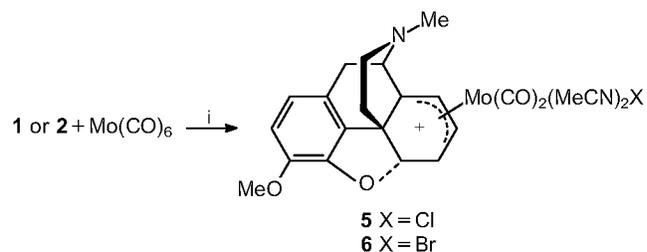
One may suggest that the π -allylic complex **A** is formed as intermediate followed by reductive elimination of Fe(CO)₃ and HX to give **3**. Compound **3** subsequently reacts with Fe(CO)₃ to give **4** (Scheme 2).



Scheme 2

In a continuation of our research into the field of synthesis of η^3 -allyl metal complexes of morphine alkaloids we have investigated the possibility of complexation of compounds of molybdenum with substituted codeines. The η^3 -allyl ligand is an ubiquitous carbon ligand in organometallic chemistry, and a variety of η^3 -allyl complexes of manganese, iron, molybdenum and tungsten are of central importance in a number of synthetically useful processes.⁷

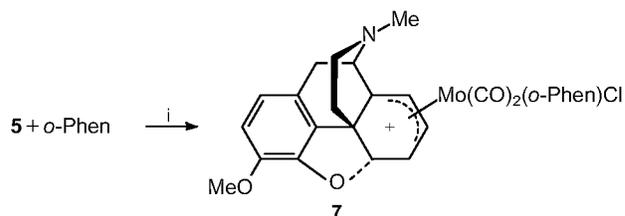
We have found that reaction of **1** or **2** with Mo(CO)₆ leads to complex **5** or **6** (Scheme 3).



Scheme 3 Reagents and conditions: i, MeCN, 80 °C, 4 h.

The same compounds (**5** and **6**) were obtained by reaction of Mo(CO)₃(MeCN)₃ with **1** or **2**.

In complexes **5** and **6** the acetonitrile ligands are labile and may be replaced by other π -donors. For example, reaction of **5** with 1,10-phenanthroline results in the exchange of the acetonitrile ligands to give complex **7** (Scheme 4).



Scheme 4 Reagents and conditions: i, benzene, 80 °C, 3 h.

These are the first examples of π -complexes of derivatives of codeine with molybdenum.

All new complexes gave satisfactory analytical and spectroscopic data.[†]

[†] 4: m.p. 129 °C; IR (KBr): 2040, 1980 1960 (C=O) cm^{-1} ; ¹H NMR (200 MHz, CDCl_3): δ 2.42 (s, 3H, MeCN), 3.76 (s, 3H, MeO), 4.51 (d, 1H, $J = 3.2$ Hz, H-8), 4.75 (d, 1H, $J = 3.5$ Hz, H-5), 5.12–5.46 (m, 2H, H-6, H-7), 6.55 and 6.65 (2d, $J = 8.2, 8.2$ Hz, H-1, H-2).

5: yield 58%; m.p. 250–252 °C (decomp.); IR (KBr): 1946, 1858 (C=O) cm^{-1} ; ¹H NMR (200 MHz, CDCl_3): δ 2.05 (br.s, 6H, 2MeCN), 2.43 (s, 3H, MeN), 3.77 (s, 3 H, MeO), 3.95 (m, 1H, H-6), 4.42 (d, 1H, $J = 2.7$ Hz, H-5), 5.20–5.85 (m, 1H, H-6), 4.42 (d, 1H, $J = 8.2, 8.2$ Hz, H-1, H-2).

6: yield 51%; m.p. 255–257 °C (decomp.); IR (KBr): 1940, 1850 (C=O) cm^{-1} ; ¹H NMR (200 MHz, CDCl_3): δ 2.10 (br.s, 6H, 2MeCN), 2.43 (s, 3H, MeN), 3.76 (s, 3H, MeO), 3.85 (m, 1H, H-6), 4.60 (d, 1H, $J = 2.8$ Hz, H-5), 5.10–5.65 (m, 2H, H-7, H-8), 6.53 and 6.62 (2d, $J = 8.2, 8.2$ Hz, H-1, H-2).

7: yield 72%; m.p. 261–262 °C (decomp.); IR (KBr): 1932, 1848 (C=O) cm^{-1} ; ¹H NMR (200 MHz, CDCl_3): δ 2.43 (s, 3H, MeN), 3.77 (s, 3H, MeO), 3.90 (m, 1H, H-6), 4.33 (d, 1H, $J = 2.7$ Hz, H-5), 5.25–5.80 (m, 2H, H-7, H-8), 6.51 and 6.60 (2d, $J = 8.2, 8.2$ Hz, H-1, H-2), 7.50 (m, 2H, H-3, H-8, *o*-Phen), 7.70 (s, 2H, H-5, H-6, *o*-Phen), 8.18 (d, 2H, $J = 7.3$ Hz, H-4, H-7, *o*-Phen), 9.22 (d, 2H, $J = 4.7$ Hz, H-2, H-9, *o*-Phen).

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