Synthesis of π-Complexes of Codeine with Iron and Molybdenum

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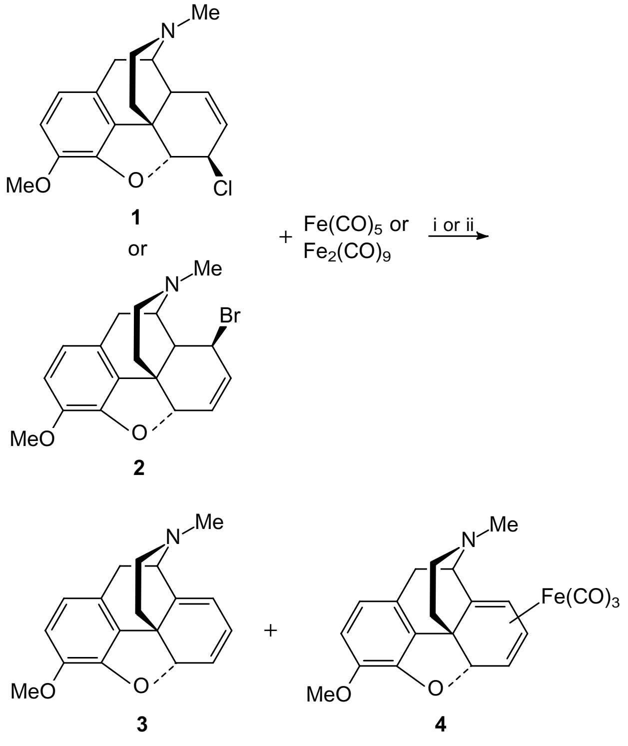
Treatment of 6β-chloro-6-deoxycodeine **1** or 8β-bromo-8-deoxypseudocodeine **2** with $Fe(CO)_5$ or $Fe_2(CO)_9$ yields 6-demethoxythebaine **3** and the π-diene iron complex **4**; compound **1** or **2** reacts with $Mo(CO)_6$ to give the π-allylic molybdenum complexes **5** and **6**, respectively.

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 palladium[4] 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.

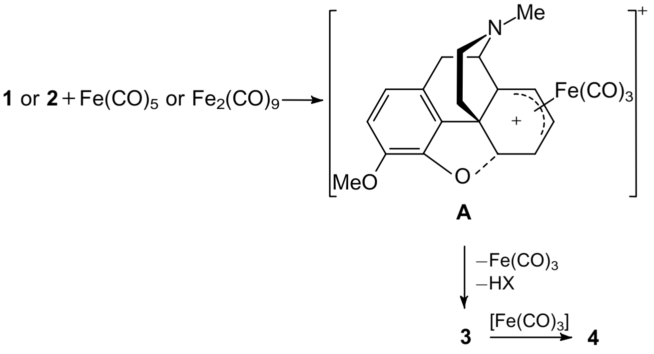
We have found that 6β-chloro-6-deoxycodeine **1** or 8β-bromo-8-deoxypseudocodeine **2** reacts with an equimolar amount of $Fe(CO)_5$ or $Fe_2(CO)_9$ to give two products: 6-demethoxythebaine **3**[5,6] and π-diene complex **4** (Scheme 1).



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, $Fe_2(CO)_9$, 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 $Fe_2(CO)_9$. Increasing the amount of $Fe(CO)_5$ or $Fe_2(CO)_9$ leads to an increase of the amount of **4**, and with a large excess of $Fe(CO)_5$ or $Fe_2(CO)_9$ **4** was formed exclusively.

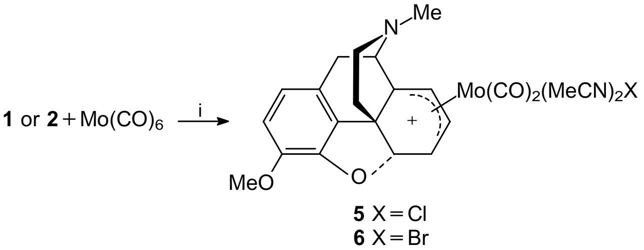
One may suggest that the π-allylic complex **A** is formed as intermediate followed by reductive elimination of $Fe(CO)_3$ and HX to give **3**. Compound **3** subsequently reacts with $Fe(CO)_3$ to give **4** (Scheme 2).



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]

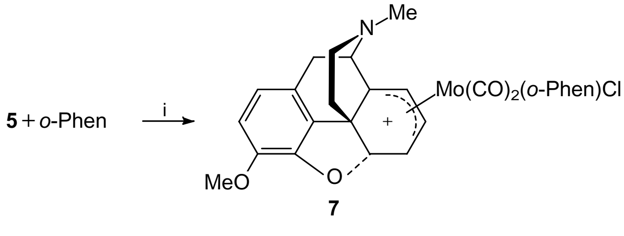
We have found that reaction of **1** or **2** with $Mo(CO)_6$ leads to complex **5** or **6** (Scheme 3).



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.[†]

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References

1 V. N. Kalinin and N. I. Kobel'kova, *Zh. Vses. Khim. O-va im. D. I. Mendeleeva*, 1991, **26**, 443 (in Russian).

2 A. J. Birch, *Aust. J. Chem.*, 1969, **22**, 971.

3 A. J. Birch, L. F. Kelly and A. J. Liepa, *Tetrahedron Lett.*, 1985, **26**, 501.

4 V. N. Kalinin, I. L. Belyakova, V. V. Derunov, J. K. Park and H. Schmidhammer, *Mendeleev Commun.*, 1995, 22.

5 C. W. Hutchins, G. K. Cooper, S. Pürro and H. Rapoport, *J. Med. Chem.*, 1981, **24**, 773.

6 H. C. Beyerman, P. R. Crabbendam, T. S. Lie and L. Maat, *Recl. Trav. Chim. Pays-Bas*, 1984, **103**, 112.

7 A. J. Pearson, *Comprehensive Organometallic Chemistry*, Pergamon Press, Oxford, 1982, vol. 8, p. 939.

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[†] **4**: m.p. 129 °C; IR (KBr): 2040, 1980 1960 (C=O) cm^{-1}; ^{1}H 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-l, H-2).

5: yield 58%; m.p. 250–252 °C (decomp.); IR (KBr): 1946, 1858 (C=O) cm^{-1}; ^{1}H 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-l, H-2).

6: yield 51%; m.p. 255–257 °C (decomp.); IR (KBr): 1940, 1850 (C=O) cm^{-1}; ^{1}H 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-l, H-2).

7: yield 72%; m.p. 261–262 °C (decomp.); IR (KBr): 1932, 1848 (C=O) cm^{-1}; ^{1}H 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-l, 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).