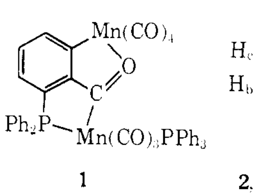
Metalation of Aromatic Ketones with Methylmanganese and Methylrhenium Carbonyl Complexes[1]

Sir:

Recent discovery of $Ph_2P[C_6H_3(CO)(Mn(CO)_4)]Mn(CO)_3PPh_3$[2] (**1**) has led us to investigate the reaction of aromatic ketones and quinones with $CH_3M(CO)_5$ (M = Mn or Re). We find that metalation of the aromatic ring in position ortho to the carbonyl group proceeds smoothly to give products such as **2** or **3**. We also find that the rate of reaction increases with decreasing carbonyl stretching frequency of the originating ketone. This is characteristic of increasing base strength of the carbonyl group[3] and, taken together with the specific metalation, leads us to believe that the entering metal is directed to the ortho position of the ring through initial donor–acceptor interaction with the carbonyl group; *cf.* directing effects of the carbonyl group in aromatic thallation[4a] or lithiation[4b] reactions.



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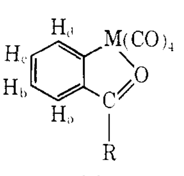
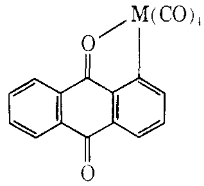


2, M = Mn or Re
R = CH_3, C_6H_5



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In a typical reaction aryl ketone and the alkylmetal carbonyl in 1:1 ratio are heated under inert atmosphere in hydrocarbon solvents at temperatures ranging from 80 to 125° and reaction times up to 12 hr; see Table I.

Table I

Compound[a]	Originating ketone	Mol wt Obsd[b]	Mol wt Calcd	$\nu_{C\equiv O}$[c]	$\nu_{>C=O\rightarrow M}$[d]
$C_{12}H_7MnO_5$, **2a**	Acetophenone	286	286	2082 m, 1997 vs 1947 s	1578
$C_{17}H_9MnO_5$, **2b**	Benzophenone	348	348	2082 m, 1997 vs 1947 s	1519
$C_{17}H_9O_5Re$, **2c**	Benzophenone	478[e]	478[e]	2096 m, 1993 s 1988 sh, 1939 s	1501
$C_{18}H_7O_6Re$, **3**	Anthraquinone	504[e]	504[e]	2096 w, 1996 s 1944 s	1512

[a] Reaction temperature, time, and solvent are as follows: **2a**, 126°, 0.5 hr, octane; **2b**, 80°, 5 hr, benzene; **2c**, 110°, 12 hr, toluene; **3**, 110°, 6 hr, toluene. [b] Mass spectral. [c] Cyclohexane solution, Beckman IR-4. [d] CCl_4 solution, Perkin-Elmer 421. [e] Based on the ^{185}Re peak of the multiplet pattern.

The progress of each reaction is followed by monitoring characteristic ir bands of starting materials and/or products in the carbonyl stretching region (*ca.* 1500–2100 cm^{-1}). Gas evolution is noted in each case. Products were purified through column chromatography (silica gel–hexane) followed by recrystallization from hexane–ether. Yields of the expected products were 60% or better.

For each product we observe a strong ir band between 1500 and 1600 cm^{-1} which is characteristic of a ketonic carbonyl group coordinated to a metal through oxygen.[5] The nmr spectrum of the product derived from acetophenone, **2a**, includes, among other features, a characteristic pattern for the ortho-metalated aromatic ring:[6] at 100 MHz and 25°, τ (ppm) (multiplicity) H_a, 2.17 (2 × 2); H_b, 2.83 (3 × 2); H_c, 2.59 (3 × 2); H_d, 1.91 (2 × 2), CH_3, 7.4 (1). Coupling constants (Hz): J_{ab}, 7.5; J_{ac}, 1.5; J_{ad}, 0.7; J_{bc}, 7.0; J_{bd}, 1.1; J_{cd}, 7.0. The assignments are based on proton decoupling experiments and nmr analysis of the analogous para and meta methyl-substituted products. The products derived fom benzophenone show similar splitting for the metalated ring when the unmetalated phenyl signal is subtracted from the spectrum. The spectrum of **3** is quite complex. Regarding the effect of substituents, the following relative rates were observed at 101° (with carbonyl stretching frequency of originating ketone given in parentheses, in cm^{-1}): for para-substituted acetophenone, *p*-OMe (1675) > *p*-Me (1680) > *p*-Cl (1686) > H (1688); for meta-substituted acetophenones, *m*-OMe (1681) > *m*-Me (1685) > H (1688); for para,para′-disubstituted benzophenones, *p,p′*-$(OMe)_2$ (1649) > *p,p′*-$(Me)_2$ (1656) $\geq$ H (1959).

The alkylmetal carbonyl derivatives of manganese and rhenium thus differ significantly in their reactivity toward substituted aromatic substrates from that reported for other transition metal complexes; methanolic Na_2PdCl_4, which will metalate aromatic rings containing nitrogen functional substituents and form simple adducts with sulfur functional derivatives, is unreactive toward aromatic ketones,[7] and a reactive intermediate derived from $(C_5H_5)_2WH_2$ and butyllithium has been shown to metalate benzophenone in the para position.[8]

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(1) Work supported by National Science Foundation (NSF) Grant No. 23267X2. Departmental instruments used in this work were supported as follows: nmr spectrometers, Varian A-60 and HA 100d, E. I. du Pont de Nemours and Co., Stauffer Chemical Co., Union Carbide Corporation, and NSF Grants No. G20207 and GP 8223; Beckman IR-4, E. I. du Pont de Nemours and Co.; AEI MS9 mass spectrometer, NSF Grant No., GP3627.

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(9) Publication No. 3196

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Received July 30, 1973

Total Synthesis and Pharmacological Activities of N-Substituted 3,14-Dihydroxymorphinans. I

Sir:

A continuing challenge in medicinal chemistry centers on the search for effective analgetics and narcotic antagonists that would be devoid of physical dependence liabilities. We initiated a program designed to prepare, by total synthesis, 3,14-dihydroxymorphinans which would hopefully combine the potent and "pure"