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DIRECT CARBOMETHOXYMETHYLATION OF ORGANOIRON AND ORGANOMANGANESE COMPLEXES USING THE REFORMATSKY REAGENT[1]

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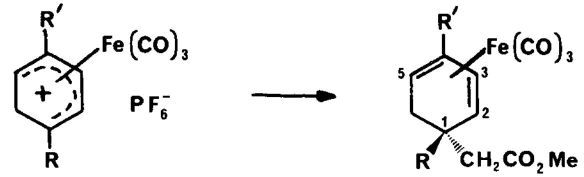
Abstract: *Reaction of* $BrZnCH_2CO_2Me$ *with cyclohexadienyl-*$Fe(CO)_3$ *and cycloheptatriene-*$Mn(CO)_3$ *salts affords products of carbomethoxymethylation in good yield.*

Synthetic applications of tricarbonylcyclohexadienyliron complexes are now well-established,[2] whilst similar applications of organomanganese derivatives remain to be discovered.[3] A large number of useful organoiron intermediates are obtained by reaction of cyclohexadienyl-$Fe(CO)_3$ complexes 1 with dimethyl malonate anion, but this requires a decarboxylation step to give monoester complexes of type 2 which, in our hands, have found application in the synthesis of a range of complex molecules.[2] Since the decarboxylation is often a tricky, variable yielding step, we sought a direct method for introduction of the CH_2CO_2R unit into these complexes.



1a R = R' = H

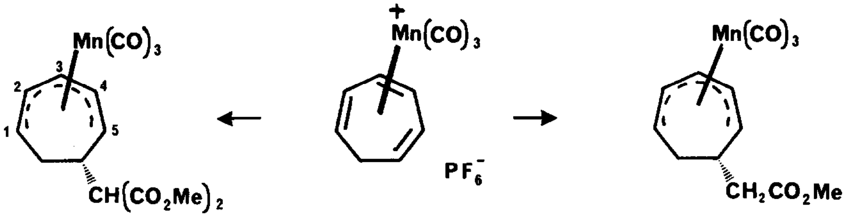
1b R = H, R' = OMe

1c R = Me, R' = OMe

2a, b, c

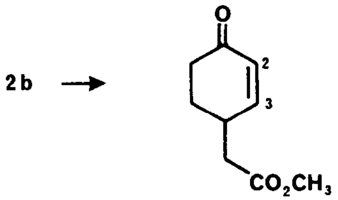
We have also recently initiated studies into the synthetic applications of triene-$Mn(CO)_3$ cations and have been similarly concerned with the attachment of terminally functionalised two carbon atom units. Whilst we found in our preliminary studies that the cycloheptatriene-$Mn(CO)_3$ hexafluorophosphate[4] 3 reacts with dimethyl potassiomalonate to give the diester complex 4 in 66% yield,[5] the sensitivity of the dienyl-$Mn(CO)_3$ system, compared to diene-$Fe(CO)_3$ precludes further manipulation of the diester grouping. Consequently, it became essential to find a direct method for introduction of the CH_2CO_2R group.

Trial studies revealed that this transformation could not be accomplished for either iron or manganese complexes using the well-known LiCH$_2$CO$_2$Bu^t. However, successful C-C bond formation occurred on treatment of the complexes with the Reformatsky reagent, BrZnCH$_2$CO$_2$Me. Thus, treatment of the manganese complex 3 with this reagent afforded the monoester 5 in essentially quantitative yield.[5] Availability of this compound should now allow us to develop some useful applications to organic synthesis.



4 3 5

Similarly, reaction of the iron complex 1a with BrZnCH$_2$CO$_2$Me gave monoester 2a in 70% yield, whilst 1b gave exclusively 2b (64%). The utility of this procedure is illustrated by the direct conversion of 2b to the 4-substituted cyclohexenone 6 on exposure to ceric ammonium nitrate (acetone-H$_2$O, 20°C).[5] Somewhat disappointingly, the disubstituted complex 1c gave a mixture of complexes 2c, 7 and 8 in a ratio of 4:1:1 (n.m.r.).



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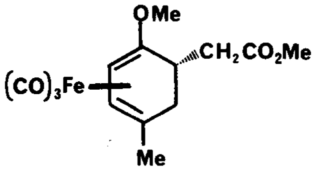

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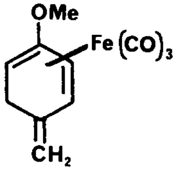

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Complex 7 arises by addition of the enolate to the unsubstituted, electronically deactivated dienyl terminus, whilst 8 results from deprotonation of the methyl group of 1c. The desired complex 2c is readily obtained pure by chromatography of the mixture followed by fractional crystallization (10% ether/hexane) m.p. 57-59°C (lit.[6] 56.5-57.5°C). Whilst the yield is rather low (ca 60-65%), we envisage that this could be considerably improved by using a 4-iso-propoxy substituent instead of methoxy as directing group, as we have demonstrated previously for other systems which give poor regioselectivity during nucleophile addition.[7]

In conclusion, we show that $BrZnCH_2CO_2Me$ is an alkylating agent for organoiron and organomanganese complexes, and the possibility of extending this to a wider range of zinc enolates is under consideration.

Typical procedure: Into a flask fitted with reflux condenser and argon balloon are placed mossy zinc (600 mg, 9.2 mmol) dry THF (50 ml) and iodine (220 mg, 0.9 mmol). The stirred mixture is heated to reflux temperature and freshly distilled methyl bromoacetate (1 ml, 10 mmol) is added dropwise. Heating is continued for 6h, after which time the mixture is allowed to cool and settle, without stirring. An aliquot of the clear supernatant (10 ml) is transferred via syringe to a dry reaction flask (under argon), cooled to 0°C, and stirred whilst solid complex 1a (300 mg) is added with backflushing of argon. Stirring is continued until the reaction is complete (40 min). Work-up with saturated aqueous $NaHCO_3$ and ether extraction in the usual way with removal of any precipitate by filtration through celite, affords the product 2a, purified by preparative t.l.c.

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3) For some recent results on arene-$Mn(CO)_3$ complexes, see: Y. K. Chung, H. S. Choi and D. A. Sweigart, J. Am. Chem. Soc., 1982, 104, 4245; Y. K. Chung, P. G. Williard and D. A. Sweigart, Organometallics, 1982, 1, 1053.
4) F. H. J. Miller, P. L. Pauson and J. B. Pd. Tripathi, J. Chem. Soc. C, 1971, 743.
5) Spectral data, etc., for new complexes are: 2a $\nu_{max}(CHCl_3)$ 2045, 1965, 1720 cm^{-1}; $\delta(CDCl_3)$

5.25 (2H,m,3-H,4-H), 3.75 (3H,s,OMe), 3.1-2.7 (3H,m,2-H,5-H,exo-6-H), 2.15 (2H,d,J 4Hz, $\mathrm{C\underline{H}_2CO_2R}$), 1.5-1.2 (2H,m,1-H, endo-6-H).

2b: ν_{max}($\mathrm{CCl_4}$) 2050, 1965, 1725, 1490 cm^{-1}; δ($\mathrm{CDCl_3}$) 5.05 (1H,dd,J6,2Hz,3-H), 3.69 (3H,s,$\mathrm{CO_2Me}$), 3.65 (3H,s,OMe), 3.23 (1H,m,5-H), 2.8-2.4 (2H,m,2-H,exo-6-H), 2.20 (2H,d,J 5Hz, $\mathrm{C\underline{H}_2CO_2R}$), 1.5-1.2 (2H,m,1-H, endo-6-H).

4: ν_{max}($\mathrm{CHCl_3}$) 2008, 1950, 1735, 1450 cm^{-1}; δ($\mathrm{CDCl_3}$) 5.81 (1H,m,3-H), 5.31 (1H,m,2-H), 4.88 (1H,m,4-H), 3.74 (3H,s,$\mathrm{CO_2Me}$), 3.68 (3H,s,$\mathrm{CO_2Me}$), 3.55 (1H, obscured, 5-H), 3.48 (1H,m,1-H), 3.01 (1H,d,J 6Hz, malonate CH), 2.07 (1H,m,6-H), 1.22 (1H,m, endo-7-H), 0.91 (1H,m, exo-7-H).

5: ν_{max}($\mathrm{CHCl_3}$) 2020, 1955, 1730, 1448 cm^{-1}, δ($\mathrm{CDCl_3}$) 5.83 (1H,dd,J 10, 5Hz, 3-H), 5.25 (1H,dd,J 7, 6Hz,2-H), 4.78 (1H,t,J 10Hz,4-H), 3.85 (1H,m, obscured, 5-H), 3.60 (3H,s,$\mathrm{CO_2Me}$),3.5-3.0 (2H, obscured, 1-H,6-H), 2.1 (2H,m,$\mathrm{C\underline{H}_2CO_2R}$ diastereotopic), 1.9 (1H,m, endo-7-H), 0.85 (1H,m, exo-7-H).

6: ν_{max}($\mathrm{CHCl_3}$) 1725, 1680, 1625 cm^{-1}; δ($\mathrm{CHCl_3}$) 6.9 (1H,m,3-H), 6.02 (1H,d,J 6Hz,2-H), 3.78 (3H,s,$\mathrm{CO_2Me}$), 2.6-1.9 (7H,m).

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