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# ORGANOMETALLICS IN ORGANIC SYNTHESIS: TRICARBONYL-(3-METHOXYCYCLOHEXA-2,4-DIEN-1-YL)-IRON(1+). A SYNTHETIC EQUIVALENT OF THE C-5 CATION OF CYCLOHEXENONE.

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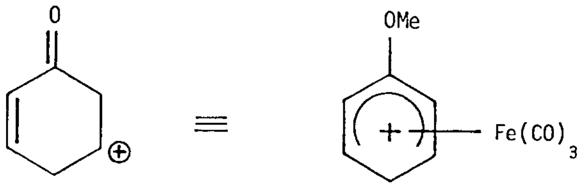
*Summary:* *Tricarbonyl-(3-methoxycyclohexa-2,4-dien-1-yl)-iron(1+) $PF_6$(1-) 2 reacts with a variety of nucleophiles to give 5-substituted cyclohex-2-enones. 2 is shown to be a useful precursor for a convergent synthesis of 5-substituted cyclohex-2-enones and to be synthetically equivalent to the 5-cyclohex-2-enone cation 1.*

The ability to elaborate cyclohex-2-en-1-one is considered important because of the widespread occurrence of its derivatives in natural products. Accordingly there exists methodology which allows direct functionalisation of this simple enone at all positions[1] with the exception of C-5 which is devoid of any endogenous activation. It is difficult for example to envisage any type of latent functionality at this position and resort is thus made to indirect methods.[2] Despite the abundance of compounds found in nature which are formally 5-substituted cyclohex-2-enone derivatives, to the best of our knowledge there have been no reports of attempts at convergent synthesis based on a synthetic equivalent of type 1.

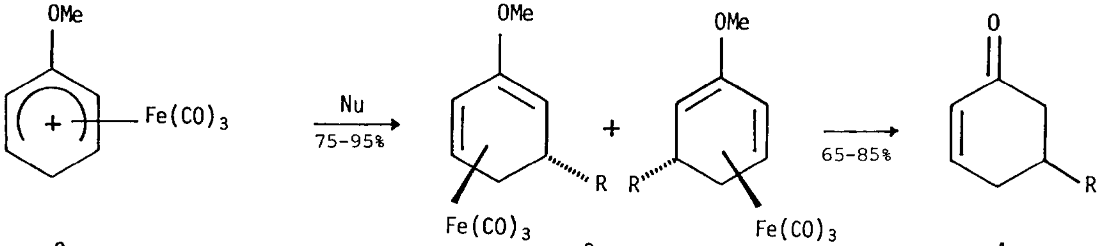


1 2

Previous work in this laboratory demonstrated the synthetic equivalence of tricarbonyl-(2-methoxycylohexa-2,4-dien-1-yl)-iron(1+) to either the C-4 cation of cyclohex-2-enone *or* the *p*-methoxyphenylcation.[3] In continuation of this theme we now describe tricarbonyl-(3-methoxycyclohexa-2,4-dien-1-yl)-iron(1+) 2 as the synthetic equivalent to 1.

2 was initially characterised by Ireland and co-workers[4] who obtained the salt as a by-product. We have utilised a four step sequence[5] to prepare the cation 2 in 70-80 g quantities and good yields.[6] While the symmetrical disposition of 2 obviates any

regiochemical problems in its reaction with nucleophiles, obvious advantages of resolved cations (cf. 2-OMe cation) are not available.

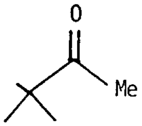
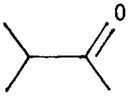
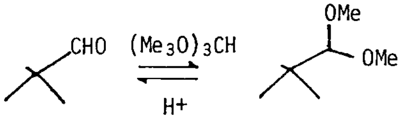
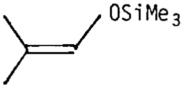
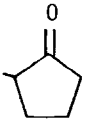
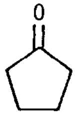
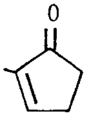
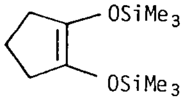


**2** **3a-g** **4a-g**

SCHEME 1

Scheme 1 indicates the reaction sequence utilized. Table 1 demonstrates some applications leading to 5-substituted cyclohex-2-enones.[7]

TABLE 1

| COMPOUND | SUBSTITUENT R | NUCLEOPHILE Nu |
|---|---|---|
| a | t-Bu | t-BuLi |
| b |  |  |
| c, d |  |  |
| e |  |  |
| f |  |  |
| g |  |  |

Conditions for the addition of the appropriate nucleophiles to cyclohexadienyl-$Fe(CO)_3$ salts have already been reported elsewhere.[8] The transformation to the cyclohexenones 4 was accomplished by treating the methoxycyclohexadieneirontricarbonyls with Jones' reagent in the case of compounds 3b, e and g or with pyridinium chlorochromate (PCC) in the case of compounds 3a, d and f. The use of PCC proves particularly advantageous for compounds such as 3d where an acetal protecting group was retained throughout the oxidation/hydrolysis reaction. 3c obtained by reacting 2 with the appropriate silylenolether in the usual way[8] was treated with the strongly acidic resin, amberlyst 15, in the presence of trimethylorthoformate (excess) in hexane solution to give the dimethyl acetal 3d in essentially quantitative yield. A solution of 3d (1 mmol) in $CH_2Cl_2$ (5 ml) was added dropwise to a stirred suspension of PCC (5 mmol) in $CH_2Cl_2$ (20 ml). After 4h the solution was poured into $Et_2O$ (200 ml) and then filtered. Evaporation of the filtrate gave crude 4d which was purified by chromatography over florisil ($Et_2O$/hexane, 1:1) (83%). The aldehyde function was easily regenerated by treatment of the acetal with amberlyst 15 resin in reagent grade $Et_2O$ (room temperature, 15 min) furnishing 4c in ≥ 95% yield. The isolation of the desired intermediates (3c,4d) in the reaction sequence 2 → 3c → 3d → 4d → 4c allows selective protection/deprotection and further manipulation of either carbonyl function in 4c.

In contrast to the recently described procedure by Semmelhack et al. involving additions of nucleophiles with $pK_a \geq 25$ to anisole-$Cr(CO)_3$ complexes[9] our results obtained with a range of nucleophiles comprising organolithium reagents, ketones, silyl enol ethers and allylsilanes indicate the generality of this approach to the synthesis of 5-substituted cyclohex-2-enones. Such compounds are vital intermediates in natural product synthesis[10] and have proved useful in controlling the stereochemistry of remote centres.[11]

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6. Details of the scaling-up of the procedure given in ref. 5(a) will be published elsewhere but are available on request.

7. Structures of all compounds in Table 1 are fully supported by spectral data (NMR, IR, Mass).

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