Regiospecific Lithiation of Permethylated (η^6-Tricarbonylchromium)phenylacetyl(tetracarbonyl)iron Anion: a Versatile Method for the α,α'-*ortho*-Bifunctionalization of Hexamethylbenzene

Jean-Jacques Yaouanc, Jean-Claude Clement, and Hervé des Abbayes*

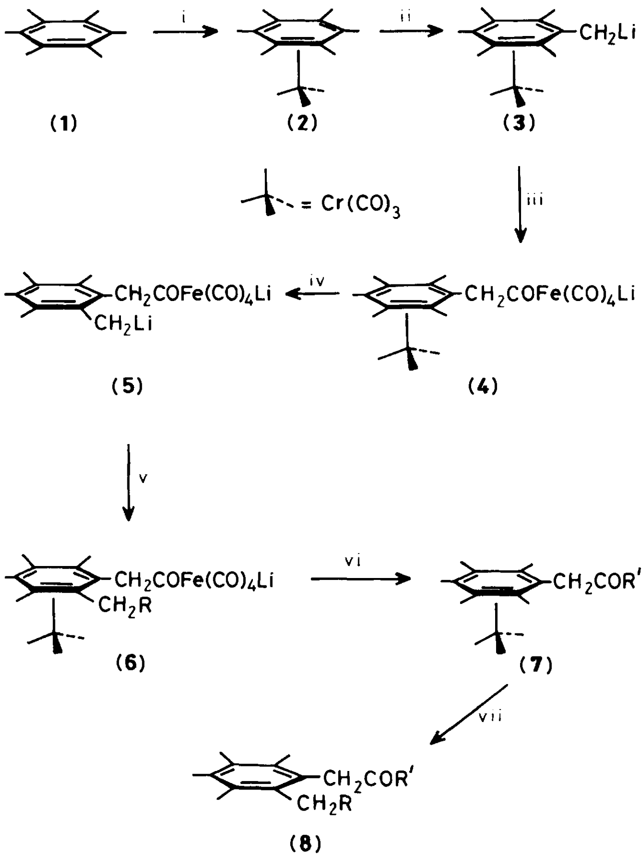
Laboratoire de Chimie Organique des Eléments de Transition, UA CNRS 322, Faculté des Sciences et Techniques de Brest (Université de Bretagne Occidentale), 6 avenue le Gorgeu, 29287 Brest Cedex, France

$Me_6C_6\{Cr(CO_3)\}$ has been converted into α,α'-*ortho*-bifunctionalized hexamethylbenzenes $(RCH_2)(R'COCH_2)Me_4C_6$ in high yields, by a sequence involving lithiation, reaction with $Fe(CO)_5$, a further lithiation, and two sequential alkylation reactions.

On co-ordination of arenes to tricarbonylchromium, either an arene ring C–H bond or a 'benzylic' C–H bond is activated towards organolithium reagents.[1] The former activation can be induced regiospecifically at an *ortho*-position by electronegative atoms bound to the complexed arene (oxygen of OMe, F, or Cl)[2] or to a 'benzylic' carbon atom (oxygen of $-CH_2O^-$).[3] We report here an unusual regiospecific activation of the latter type, *i.e.* of the C–H bond of a methyl group in an *ortho*-position, induced by the anionic acyl(tetracarbonyl)iron moiety bound to a benzylic carbon atom of the complexed permethylated arene ring. This leads to a clean and versatile method for *ortho*-bifunctionalization of hexamethylbenzene.

The reaction (Scheme 1) between hexamethylbenzene(tricarbonyl)chromium (**2**)[4] [readily available (97% yield) on complexation of hexamethylbenzene (**1**) with $Cr(CO)_6$ in refluxing di-n-butyl ether–tetrahydrofuran [(THF)] and n-butyl-lithium for 30 min at 0 °C in THF afforded the golden-yellow lithiated derivative (**3**), stable at 0 °C, which on reaction with $Fe(CO)_5$ at 0 °C for 2 h, produced the lithium salt of the acyl(tetracarbonyl)iron anion (**4**).†‡

A further reaction with n-butyl-lithium at −25 °C for 1 h resulted in the formation of a bright orange–yellow compound, stable at −25 °C and formulated as (**5**). A first reaction of RX (MeI, AcCl, $BrCH_2CH:CH_2$, or $ClCO_2Me$) acting as an electrophile resulted in alkylation at the more reactive benzylic position, giving the intermediate (**6**).‡ Further alkylation (R'X = MeI) at iron finally created the acyl group of the complex (**7**). On decomplexation of (**7**) in ethereal solution with oxygen in sunlight, the α,α'-*ortho*-bifunctionalized hexamethylbenzene (**8**) was obtained, in overall yields of 60—80% [from (**2**)] after chromatographic purification. That the two substituents RCH_2 and $R'COCH_2$ were 1,2-disposed in (**8**) was demonstrated by high resolution 75.49 MHz Fourier transform ^{13}C n.m.r.: for R = COMe and R' = Me, there are only three magnetically different arene ^{13}C atoms, and indeed only three signals were observed (δ 134.7, 132.9, and 129.5); for R ≠ COMe and R' = Me, six signals were observed (for example for R = CO_2Me, R' = Me, δ 134.7, 134.6, 133.4, 133.0, 130.0, and 129.3).



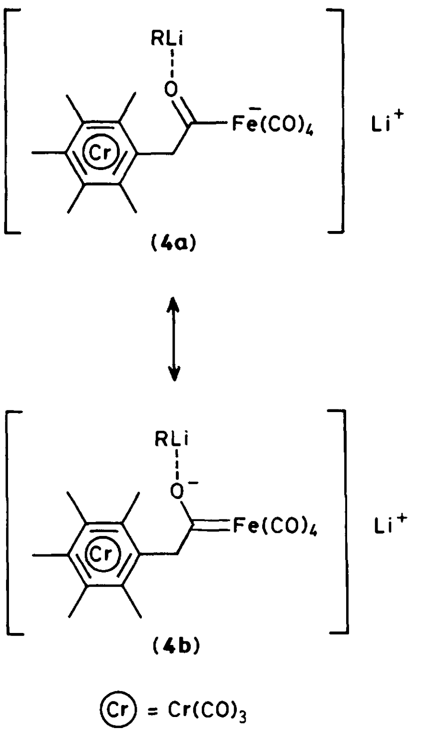
Scheme 1. *Reagents*: i, $Cr(CO)_6$; ii, Bu^nLi; iii, $Fe(CO)_5$; iv, Bu^nLi; v, RX; vi, R'X; vii, $O_2/h\nu$. For (**8a**) (R = Me, R' = Me) v, MeI; vi, MeI; for (**8b**) (R = COMe, R' = Me) v, MeCOCl; vi, MeI; for (**8c**) (R = $CH_2CH{=}CH_2$, R' = Me) v, $CH_2{=}CHCH_2Br$; vi, MeI; for (**8d**) (R = CO_2Me, R' = Me) v, $ClCO_2Me$; vi, MeI. M.p.s, *m/z* values, and yields [*vs.* (**2**)] after chromatographic purification: (**8a**) 60 °C, 217, 56%; (**8b**) 122 °C, 246, 68%; (**8c**) 53 °C, 244, 75%; (**8d**) 81 °C, 262, 78%. I.r., ^1H n.m.r., ^{13}C n.m.r., and mass spectral data are fully consistent with the proposed structures.

We think that the regiospecific lithiation of (**4**) to give (**5**) is induced by the electron-rich oxygen atom of the anionic acyl(tetracarbonyl)iron moiety.[6,7] The low i.r. absorption frequency for the acyl group of (**4a**) [THF; Li^+ counterion,

---

† Acyl(tetracarbonyl)iron derivatives of the type $Li[\eta^6\text{-}o\text{-}(CO)_4Fe(CO)XC_6H_4\{Cr(CO)_3\}]$ (X = Cl or Me) were recently obtained from the reaction of $\eta^6\text{-}o\text{-}LiXC_6H_4\{Cr(CO)_3\}$ with $Fe(CO)_5$.[5]

‡ *Pertinent data* for the anion (**4**): i.r. (THF; Li^+ counterion, cm^{-1}) ν (C≡O) 2018m, 1951s, 1901s, and 1873vs, ν (C=O) 1572br.; ^1H n.m.r. [$(Ph_3P)_2N^+$ counterion; CD_2Cl_2; 60 MHz; 25 °C) δ 4.50 (2H, s) 2.20 (6H, s), 2.13 (6H, s), and 2.07 (3H, s); $^{13}C\text{-}\{^1H\}$ n.m.r. [$(Ph_3P)_2N^+$ counterion; CD_2Cl_2; 75.49 MHz; 25 °C] δ 262.4 (C=O, s), 221.3 and 237.0 [$Fe(CO)_4$ and $Cr(CO)_6$, respectively], 109.3, 108.3, 107.7, and 107.2 (arene), 67.7 (CH_2), and 17.7, 17.6, and 17.4 (CH_3). As expected,[7] reaction of MeI with the anion (**4**) gave the methyl ketone $(Me_5C_6)CH_2COMe$ after full decomplexation (O_2; *hν*; in Et_2O) [overall yield from (**2**) 82%, m.p. 78 °C, *m/z* 204]. For the $(CO)_4Fe\text{–}C{=}O$ acyl group, the anion (**6**) exhibited the same i.r. absorption frequency [ν (C=O) 1572br. cm^{-1}; THF; Li^+ counterion] as the anion (**4**). It is well known that methyl iodide reacts at the iron atom of the anions $RCOFe(CO)_4^-$ to give ketones RCOMe.[7]



Scheme 2

ν (C=O) 1572 cm^{-1}] indicates a strong contribution of the carbenic form (**4b**). Then n-butyl-lithium should be in the right place for deprotonation of a methyl group in the *ortho*-position (Scheme 2).

Overall, the reactions shown in Scheme 1 constitute a very efficient method for regiospecific α,α'-*ortho*-bifunctionalization of hexamethylbenzene. Other regiospecific lithiations induced by the anionic acyl(tetracarbonyl)iron group are under investigation.

Received, 11th May 1988; Com. 8/01854E

References

1 J. P. Collman, L. S. Hegedus, J. R. Norton, and R. G. Finke, 'Principles and Applications of Organotransition Metal Chemistry,' University Science Books, Mill Valley, California, 1987, p. 921.
2 M. F. Semmelhack, J. Bisaha, and M. Czarny, *J. Am. Chem. Soc.*, 1979, **101**, 768.
3 J. Blagg, S. G. Davies, C. L. Goodfellow, and K. H. Sutton, *J. Chem. Soc., Chem. Commun.*, 1986, 1283.
4 (a) E. D. Fischer, K. Öfele, W. Fröhlich, H. Essler, P. Mortensen, and W. Wemmlinger, *Chem. Ber.*, 1958, **91**, 2763; (b) B. Nicholls and M. C. Whiting, *J. Chem. Soc.*, 1959, 551; (c) W. R. Jackson, B. Nicholls, and M. C. Whiting, *ibid.*, 1960, 469.
5 J. A. Heppert, M. E. Thomas-Miller, P. N. Swepston, and M. W. Extine, *J. Chem. Soc., Chem. Commun.*, 1988, 280.
6 W. O. Siegl and J. P. Collman, *J. Am. Chem. Soc.*, 1972, **94**, 2516.
7 J. P. Collman, R. G. Finke, J. N. Cawse, and J. I. Brauman, *J. Am. Chem. Soc.*, 1978, **100**, 4766.