**PAPER** 

Cite this: New J. Chem., 2011, 35, 2375-2381

# A combined experimental-theoretical study on the lithiation/electrophilic quench reaction of benzylic position of $(\eta^5$ -tetramethylcyclohexadienyl)-Mn(CO)<sub>3</sub>†‡

Eric Rose,\*<sup>a</sup> Julien Dubarle-Offner,<sup>a</sup> Françoise Rose-Munch<sup>a</sup> and Hélène Gérard\*<sup>b</sup>

*Received (in Montpellier, France) 28th February 2011, Accepted 16th August 2011* DOI: 10.1039/c1nj20178f

An  $[(\eta^{6}-1,2,4,5-\text{tetramethylbenzene})Mn(CO)_3]^+ BF_4^-$  complex treated with hydride gives a neutral  $(\eta^{5}-1,2,4,5-\text{tetramethylcyclohexadienyl})Mn(CO)_3$  complex whose X-ray analysis is described. Functionalization of the latter complex at a "benzylic" position using a lithiation/ electrophilic quench sequence affords two regioisomers of which the major one corresponds to the functionalization at the C9 carbon. Theoretical computations show that the regioselectivity of lithiation is governed by the stability of the carbanion and thus by its conjugation.

#### Introduction

The presence of the electron-deficient  $Cr(CO)_3$ ,  ${}^1[Mn(CO)_3^+]^2$  or  $[(C_5H_5)Fe^+]^3$  fragment attached to an arene ring decreases the electronic density of the arene and enhances the electrophilic character of the ligand as well as the acidity of its protons. Thus, addition of a nucleophile Nu<sup>-</sup> to neutral ( $\eta^6$ -arene)Cr(CO)\_3 and isoelectronic cationic ( $\eta^6$ -arene)-Mn(CO)\_3^+ or -FeCp<sup>+</sup> complexes leads to the formation of anionic [( $\eta^5$ -6-Nu-cyclohexadienyl)Cr(CO)\_3^-]<sup>1a,1c</sup> which can be stabilized by trapping with ClSnPh<sub>3</sub> (Scheme 1a), <sup>4</sup> and of stable neutral *exo*-substituted ( $\eta^5$ -6-Nu-cyclohexadienyl)-[M] complexes [M] = Mn(CO)\_3 or -Fe(C<sub>5</sub>H<sub>5</sub>)<sub>2</sub> (Scheme 1b). The chemistry of Cr<sup>5</sup> and Mn<sup>6</sup> complexes has been extensively developed by our group which opened an access to a wide range of organometallic molecules.

Recently, we wondered whether the lithiation/electrophilic quench sequence method which allows functionalization of the ring of  $(\eta^5$ -cyclohexadienyl)Mn(CO)<sub>3</sub> complexes<sup>6c</sup> could be applied to substitute "benzylic" positions, *i.e.* the positions alpha to the  $\eta^5$ - $\pi$  system. Indeed, the study of the benzylic position has already been reported for the cationic  $[(\eta^6$ -alkylarene)Mn(CO)<sub>3</sub>]<sup>+</sup>



Scheme 1 Addition of Nu<sup>-</sup> to (a)  $(\eta^{6}\text{-arene})Cr(CO)_{3}$  complexes, (b) M = Mn(CO)\_{3}^{+}, Fe(C<sub>5</sub>H<sub>5</sub>)<sup>+</sup>.

complexes<sup>7</sup> and has been well developed in the  $(\eta^{6}\text{-arene})Cr(CO)_{3}$ series<sup>8</sup> as well as in the  $[(\eta^{6}\text{-alkylarene})(\eta^{5}C_{5}H_{5})]Fe^{+}$  series.<sup>9</sup> Deprotonation of organometallic complexes at a benzylic position of  $[(\eta^{6}\text{-alkylarene})Mn(CO)_{3}]^{+}$  complexes readily occurred using a large excess of a strong base.<sup>7e,7f</sup> The authors observed the formation of  $(\eta^{5}\text{-pentamethylbenzyl})Mn(CO)_{3}$  complexes presenting a highly activated exocyclic double bond (Scheme 2).

Very recently, we reported a lithiation/electrophilic quench sequence at a "benzylic" position of  $(\eta^5$ -tetramethyl) and  $(\eta^5$ -pentamethyl)-6-*exo*-phenylcyclohexadienyl)Mn(CO)<sub>3</sub> complexes **3** and **4** obtained by addition of PhMgBr to  $(\eta^6$ -tetramethyl)- and  $(\eta^6$ -pentamethyl)-benzeneMn(CO)<sub>3</sub><sup>+</sup> complexes **1** and **2** (Scheme 3).

In both cases, as evidenced by NMR and X-ray analyses, we observed a regioselective deprotonation at the methyl groups C9 or C10 (Scheme 3) substituting the C2 or C4 carbons of the cyclohexadienyl ring eclipsed by a Mn–CO bond by trapping the lithiated product with different electrophiles (ClSiMe<sub>3</sub>, PPh<sub>2</sub>Cl and DMF).<sup>10</sup>

<sup>&</sup>lt;sup>a</sup> UPMC Univ Paris 06, Institut Parisien de Chimie Moléculaire IPCM, CNRS UMR 7201, Equipe de Chimie Organique et Organométallique, Bât. F, Case 181, 4, Place Jussieu, F-75252 Paris Cedex 05, France. E-mail: eric.rose@upmc.fr; Tel: +33 (0)144276235

<sup>&</sup>lt;sup>b</sup> UPMC Univ Paris 06, Laboratoire de Chimie Théorique, CNRS UMR 7616, Tour 12-13, 4<sup>eme</sup> étage, Case 137, 4, Place Jussieu, F-75252 Paris Cedex 05, France. E-mail: helene@lct.jussieu.fr

<sup>†</sup> Dedicated to Prof. Didier Astruc on the occasion of his 65th birthday.

<sup>&</sup>lt;sup>‡</sup> Electronic supplementary information (ESI) available: Tables listing detailed X-ray crystallographic data of complex 7 and Cartesian coordinates and electronic energies for compounds 7 and 8 in neutral, deprotonated and lithiated forms. CCDC reference number 812616. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1nj20178f



Scheme 2 Deprotonation of  $[(\eta^6-alkylarene)Mn(CO)_3]^+$  complexes.



**Scheme 3** Lithiation of  $(\eta^5$ -tetramethyl)- and  $(\eta^5$ -pentamethylcyclohexadienyl)tricarbonylmanganese complexes.



Scheme 4 Theoretically studied complexes.

Here we report on the synthesis and structure of the  $(\eta^{5}, 1, 2, 4, 5$ -tetramethylcyclohexadienyl)Mn(CO)<sub>3</sub> complex 7 bearing two hydrogen atoms at the sp<sup>3</sup> carbon and the study of its deprotonation. The results obtained are then analyzed on a theoretical basis using computations on the lithiation products of compound 7 compared to those of pentamethyl derivative 8 and non-methylated compound 9 (Scheme 4). Steric effects due to the Ph group substituting H at C6 in 7 (yielding, respectively, compound 3) are also examined (see below).

# **Results and discussion**

The  $[(\eta^{6}-1,2,4,5-\text{tetramethylbenzene})Mn(CO)_3]^+ BF_4^- \text{ complex 1}$ , obtained in 90% yield using the "silver (1) method" with BrMn(CO)\_5 and AgBF\_4^- and the corresponding free arene, <sup>10,11</sup> treated with LiAlH<sub>4</sub> afforded the ( $\eta^5$ -tetramethyl-cyclohexadienyl)Mn(CO)\_3 complex 7 in 66% yield. Pleasingly, monocrystals of complex 7 were readily obtained by slow evaporation of a diethylether/pentane solution of the complex. The ORTEP view shown in Fig. 1 indicates an  $\eta^5$ -cyclohexadienyl structure, with five coplanar sp<sup>2</sup> carbons and the remaining sp<sup>3</sup> carbon located 42.6(1)° above this plane. The conformation of the Mn(CO)\_3 tripod is in agreement with what is usually observed, the sp<sup>3</sup> carbon being eclipsed by one Mn–CO bond.<sup>2/,2g,6/</sup> The Mn–C bond lengths lie in the range 2.1145(15) to 2.2235(16) Å with the Mn–C3 bond being the shortest one. Crystal data are gathered in Table 1.

A lithiation/electrophilic quench sequence was performed on  $(\eta^{5}-1,2,4,5-tetramethylcyclohexadienyl)Mn(CO)_{3}$  complex 7 under the same experimental conditions as those for deprotonation of benzylic positions of  $\eta^{5}-6exo$ -Ph-methylcyclohexadienyl



**Fig. 1** Molecular structure of complex 7 with thermal ellipsoids at the 50% probability level. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Mn–C1: 2.2218(16); Mn–C2: 2.1536(15); Mn–C3: 2.1145(15); Mn–C4: 2.1575(15); Mn–C5: 2.12335(16); Mn–C6: 2.7445(19); C1–C2: 1.396(2); C2–C3: 1.414(2); C3–C4: 1.419(2); C4–C5: 1.389(2); C5–C6: 1.506(2).

	Complex 7
Empirical formula	C <sub>13</sub> H <sub>15</sub> MnO <sub>3</sub>
Formula weight	274.19
Temperature/K	200(2)
Wavelength/Å	0.71073
Crystal system	Monoclinic
Space group	$P2_1/c$
a/Å	11.887(1)
b/Å	9.228(2)
c/Å	12.585(3)
$\alpha/^{\circ}$	90
$\beta/^{\circ}$	108.932(7)
$\gamma/^{\circ}$ .	90
$V/\text{\AA}^3$	1305.8(4)
Z	4
$D_{\text{calculated}}/\text{mg m}^{-3}$	1395
$\mu/\mathrm{mm}^{-1}$	1.004
F(000)	568
Crystal size/mm	$0.3 \times 0.15 \times 0.1$
Diffractometer	к-CCD
$\theta$ range/°	3.62 to 30.00
Limiting indices	$-16 \le h \le 13$
	$-12 \le k \le 8$
	$-17 \leq l \leq 17$
Reflections collected/unique	10505/3772[R(int) = 0.0303]
Refinement method	Full matrix square on $F^2$
Data/restraints/parameters	3772/0/158
Goodness-of-fit on $F^2$	1.05
Final <i>R</i> indices $[I > 2\sigma(I)]$	$R^{1} = 0.0333$
	$wR^2 = 0.0727$
R indices (all data)	$R^{1} = 0.0593$
° •	$wR^2 = 0.0801$
Largest difference in peak/hole [e $A^{-3}$ ]	0.297 and -0.234
CCDC deposition number	812616

derivatives 3 and 4.<sup>10</sup> It appeared that deprotonation of complex 7 could be achieved at low temperatures and that the corresponding "benzylic" carbanion was stable up to -20 °C. The best conditions for this lithiation/electrophilic quench sequence correspond to the following protocol. Introduction of 4 equivalents of *n*BuLi and TMEDA at -40 °C in solution of complex 7 in THF, 1 h at -40 °C, then introduction of the electrophile, again 1 h at -40 °C followed by warming the reaction mixture to rt within 1 h. Chlorotrimethylsilane and chlorodiphenylphosphine were tested as electrophiles. Chromatography on silica gel afforded in each case two mono-functionalized regioisomers at the C7 and C9 carbons in the 3:1 ratio



Scheme 5 Lithiation/electrophilic quench sequence on complex 7.

as evidenced by NMR spectroscopy. These new complexes **10**, **11** and **12**, **13**, which could not be separated, were isolated in 73 and 82% yields respectively (Scheme 5). As previously observed, no product due to the lithiation of the cyclohexadienyl ring at the C3 carbon was formed.

The origin of the experimentally observed regioselectivity was examined using theoretical computations on the lithiation products (Schemes 3 and 4) of tetramethyl derivatives 3 and 7. Comparison to the pentamethylated derivatives 4 and 8 and to the compound without the methyl group 9, which was examined in our previous studies,<sup>6d</sup> will be proposed for better understanding.

In a first step, the three complexes 7, 8 and 9 were geometrically optimized and their geometric, energetic and electronic properties were examined to evaluate the effect of the Me substituents on the geometrical properties of these species (Table 2 and Cartesian coordinates in ESI<sup>‡</sup>). In all three cases, the distances of the Mn center to the cyclohexadienyl carbon atoms decrease as the carbon is further from the sp<sup>3</sup> center; in addition, the distances for a given carbon lie within 0.03 Å between the three complexes, which highlights the small effect of the Me groups on the geometrical properties of the cyclohexadienyl moiety. In contrast, a clear cut electronic effect is evidenced using charge and frequency analysis. The larger the number of methyl groups the more negative the charge at the Mn(CO)<sub>3</sub>

**Table 2** Mn–C distances (in Å), Mülliken  $(q_M)$  charges of the Mn(CO)<sub>3</sub> moiety (in electrons) and the three harmonic  $\nu_{CO}$  vibrational frequencies (in cm<sup>-1</sup>, repeated when equal from degeneracy) for three of the complexes described in Scheme 5

7	8	9
2.282 2.200 2.144 -1.34 2008 2010	2.267 2.193 2.170 -1.44 2005 2006	2.265 2.172 2.158 -0.88 2024 2024
	7 2.282 2.200 2.144 -1.34 2008 2010 2072	7     8       2.282     2.267       2.200     2.193       2.144     2.170       -1.34     -1.44       2008     2005       2010     2006       2072     2068

**Table 3** Energies (in kcal mol<sup>-1</sup>, computed with respect to the *cis* product with Li at the C7 benzylic carbon) of the lithiated regioisomers at the C7, C9 and C3 carbons of **7** and at C7, C9 and C11 of **8** for the two possible spatial arrangements as well as energies computed with respect to the anionic product deprotonated at the C7 benzylic carbon of the anionic form optimized in the absence of any Li<sup>+</sup> counterion. Energies in parentheses are computed in the presence of a continuum model for solvation by THF

	Regio.	C7	C9	C3	C11
7	Trans Cis	11.7 (6.8)	16.3 (14.7)	19.2 (20.2)	_
0	Anion	0.0 (0.0)	10.5 (12.1) 12.4	36.7	21.0
0	Cis Anion	0.0	10.7		16.2 16.7

center<sup>12</sup> and, coherently, the smaller the CO vibrational frequencies. This highlights the noticeable donor effect of the Me groups toward the cyclohexadienyl unit and thus to the manganese atom.

Reaction products of these three complexes toward lithiation were then examined. In order to represent to the best the experimentally formed species, benzylic H atoms number 7, 9 and 11, Scheme 4, were replaced by a Li cation coordinated to a Me<sub>2</sub>N–CH<sub>2</sub>–CH<sub>2</sub>–NMe<sub>2</sub> ligand (TMEDA) so that both steric and electronic effects are evaluated. Under these conditions, no additional molecule can be added to lithium due to the steric hindrance of the TMEDA ligand so that further explicit solvation of the molecule is necessary.

When lithiation takes place at a benzylic carbon, two coordination modes can be proposed for the lithium cation: either under the cyclohexadienyl plane, *cis* to the Mn(CO)<sub>3</sub> moiety, or above the cyclohexadienyl unit *trans* to the Mn(CO)<sub>3</sub> tripod. When lithiation takes place at the arylic position (C3 in 7), the lithium cation lies within the cyclohexadienyl plane and only one isomer is obtained. Both arrangements were computed in the case of **7** and **8** for the three possible regioisomers and results are gathered in Table 3, represented in Fig. 2 and Cartesian coordinates are given in ESI.<sup>‡</sup>

Considering the *cis/trans* spatial arrangement of the lithium binding, it appears that the lithiation product *cis* to the Mn(CO)<sub>3</sub> moiety is always more stable than the *trans* one. In contrast, shorter Li–C bonds are observed for the *trans* conformers (between 2.08 and 2.18 Å) than for the *cis* conformers (between 2.21 and 2.34 Å). This side preference is found to be unaffected by the adjunction of a continuum model for solvation by THF. This conformation preference can be easily understood on the basis of the electrostatic properties of the complexes **7** and **8**, as illustrated by the dipole moment and the electrostatic potential associated with complex **8** (see Fig. 3): the side of the ring *trans* to the Mn(CO)<sub>3</sub> moiety is the more positively charged<sup>13</sup> and on the positive side of the dipole so that binding of the lithium cation is clearly preferred *cis* to the Mn(CO)<sub>3</sub> moiety.

Transfer of this side preference from the H substituted 7 and 8 to 3 and 4, where C6 is substituted by R' = Ph instead of H, is straightforward as the less stable conformer (*trans*) is also more destabilized by the steric hindrance due to the Ph substituent. Quantitative evaluation of steric effects between the R' group and the Li(TMEDA) moiety is nevertheless



**Fig. 2** *Cis* and *trans* spatial arrangements of the regioisomers of Table 3 (a) 7, (b) 8 (energies in kcal  $mol^{-1}$  in parentheses).

obtained. This is done by examining the stabilities of the two regioisomers in the *trans* arrangement (Li at C7 and C9) relative to that of the regioisomer with Li at C3 in compounds 7 ( $\mathbf{R}' = \mathbf{H}$ , no steric effect expected) and 3 ( $\mathbf{R}' = \mathbf{Ph}$ , Table 4). Indeed in these reactants, lithiation in position 3 takes place at



Fig. 3 Electrostatic properties of 8. (a) Electrostatic potential mapped on the electron density isosurface (isodensity value = 0.04, more positive regions in blue and more negative regions in red). (b) Dipole moment direction (carbon atoms in green, hydrogen in white, oxygen in red and manganese in blue).

**Table 4** Effect of the substituent R' at C6 on the relative energies of the lithiation products of **3** and **7** in the *trans* arrangement (computed with respect to the product of lithiation of Li at the C7 carbon in the *trans* form, in kcal mol<sup>-1</sup>)

	R′	Li at C7	Li at C9	Li at C3
7	H	0.0	+4.6 + 3.2	+ 7.5
3	Ph	0.0		+ 7.6

the arylic position, for which only one arrangement is possible (lithium bonded in the plane), and little steric effects between R' and the Li(TMEDA) moiety are expected. As little or no change in the energy difference between Li at the carbon C7 and Li at the carbon C3 or C9, Table 4, can be observed upon transformation of a R' = phenyl into a R' = hydrogen in the *trans* products, it can be concluded that there is no significant steric effect between Li(TMEDA) and the phenyl substituent located at C6. As no effect of R' is found in the case of the *trans* product and as no effect is expected in the *cis* ones, the change in the regioselectivity of the reaction observed experimentally when replacing a phenyl group by a hydrogen cannot be justified by the difference in the stability of the lithiation product.

Lithiated products in the cis arrangement will thus be considered in the rest of our study. The relative stabilities of the three regioisomers are the following: Li7 < Li9 < Li3(where < stands for "more stable"). This order is found to be unaffected by inclusion of implicit solvation in the case of compound 7 (see Table 3). The product lithiated in position 7 is preferred by over 10 kcal mol<sup>-1</sup>, which should be associated to a fully selective lithiation in this position if this intermediate is the source for regioselectivity. As this preference is expected to be independent of the nature of the substituent at C6 (see above), recovery of products substituted in position 7 should be favoured under thermodynamic control of the lithiation step for both 7 and 8. Comparison of experimental results gives interesting insights within these results. Indeed, from computational data, lithiation on the benzylic carbon 7 or 8 should always be preferred, either for 3 and 7 or for 4 and 8. As the energy difference between the most stable intermediate and the other possible one is large, we can trust the computationally predicted selectivity and thus propose that recovery of products substituted on the carbon 9 or 10 results from a kinetically controlled lithiation sequence. These kinetic products are the sole

products in the presence of a  $\mathbf{R}' = \mathbf{phenyl}$  in position 6 on the cyclohexadienyl moiety (Scheme 3). When  $\mathbf{R}' = \mathbf{H}$ , further equilibration of the kinetic product, *i.e.* the product of lithiation at C9 or C10, leads to the 3/1 ratio of products as shown in Scheme 5. This equilibration is believed to be incomplete.

We learned more about this regioselectivity by performing the reaction using ClSiMe<sub>3</sub> as an electrophile at lower temperature. Indeed, at -78 °C, instead of -40 °C, the NMR spectrum of the crude mixture indicates the presence of only one regioisomer **11** at the C9 carbon, in the presence of the starting material as the major product. This confirms that lithiation at the benzylic carbon C9 is under kinetic control while the preference for the lithiation at the benzylic carbon C7 results from a thermodynamic control.<sup>14</sup>

Another remarkable point is that lithiation at the site opposite to the sp<sup>3</sup> carbon is disfavoured over all other lithiations, whatever the compound (and thus the nature of the site, arylic *vs* benzylic) at stake. Both benzylic C11 and arylic C3 lithiations are disfavoured by 19.2 and 16.2 kcal mol<sup>-1</sup>, respectively, with respect to the lithiation in position C7 (Table 3). This justifies the total absence of substitution at the carbon C3 in the course of the experimental procedure.

Understanding of the high energies for regioisomers lithiated at C3 and C11 was obtained by decomposing the lithiation process energies in two effects: (i) impact of the lithium counterion; (ii) intrinsic stability of the deprotonated species. In order to apply this decomposition scheme, the deprotonated species have been computed (Cartesian coordinates are given in ESI<sup>†</sup>) and their relative stabilities are compared to those of the lithiated species. As shown in Table 3, the relative stabilities of the anions in 8 (0.0, 12.2 and 16.7 kcal mol<sup>-1</sup> for the C7, C9 and C11 deprotonated species respectively) follow exactly those of the cis lithiated species in 8 (0.0, 10.7 and 16.2 kcal  $mol^{-1}$  for the C7, C9 and C11 lithiated species respectively) whereas in 7 additional destabilization (from +19.2 to +36.7 kcal mol<sup>-1</sup>) is obtained in position 3 only by removing the counterion: lithium coordination to the arylic position is thus more stabilizing than to the benzylic position. This is associated to a shorter Li–C bond in the arylic position (2.04 Å) compared to those obtained in the benzylic position, either in *trans* (2.08 Å) or even more in cis (2.21 Å) conformations. This can be connected to delocalization of the lone pair when deprotonation takes place in the benzylic position: the electrons of the carbanion are thus less adapted to ensure lithium binding. This is in line with the long Li-C distances observed in this compound, characteristic of clearly ionic and delocalized Li...C distances. Another origin can be the strong elongation and thus partial breaking of the Mn...arylic carbon bond observed upon deprotonation at the corresponding benzylic position.14

Nevertheless, the major effect determining the relative stability of the lithiated species is the intrinsic stability of the carbanion formed. This effect (referred to ii in the paragraph above) can be examined using isodesmic reactions allowing us to compare the deprotonation of species 7 or 8 with that of the analogue 9 bearing no methyl group at all on the cyclohexadienyl ring, which is used as a reference (Fig. 4). The aim of this reaction is not to reproduce a true chemical process but to compare the relative stability of the anionic forms. The adjunction of the



Fig. 4 Deprotonation energies (kcal mol<sup>-1</sup>) for compounds 9, 7 and 8 in positions C3 and C11. For 8 (2 bottom lines) the transition state (TS) for rotation of the  $CH_2^-$  moiety is used as an intermediate state to decompose the overall deprotonation in two steps.<sup>6d,15</sup>

four Me groups does not alter significantly the stability on the anion in the arylic position 3 as shown by the very small energy for the isodesmic proton exchange reaction between deprotonated 9 and 7. In conclusion, thermodynamically, the anionic structure is not less stable in 7 than it is in 9. for which deprotonation in position 3 was observed experimentally together with deprotonation in position 2 in the ratio 20:80.<sup>6d</sup> The proton exchange between the arylic position in 9 and the benzylic position in 8 is then examined (Fig. 4, bottom). The benzylic anion is found to be favoured by nearly 20 kcal  $mol^{-1}$  over the arylic position. The origin of this preference can in turn be decomposed in two terms, as shown by the cycle at the bottom of Fig. 4. A structure, in which there is no conjugation of the carbanion with the ring as the CH<sub>2</sub> moiety is perpendicular to the cyclohexadienyl plane, has been located: 6d,15 it is searched as a transition state for rotation along the C3-C11. The minimum is the conjugate form and the transition state the non-conjugated one, the difference between both can be used as an evaluation of the conjugation energy of the anionic double pair with the cyclohexadienyl moiety. A 34.1 kcal mol<sup>-1</sup> value is found for conjugation (Table 5 and Fig. 4). The energy for the proton exchange between this transition state anion and 9 can thus be considered as the energy difference between abstraction of a  $H^+$  from a non-conjugated sp<sup>3</sup> carbon and a sp<sup>2</sup> carbon. As expected, the  $sp^2$  anion is the more stable structure by 15.1 kcal  $mol^{-1}$ . The negative value for the isodesmic reaction for proton transfer between the anionic form of 9 and 8 is thus due to the stabilization of the carbanionic form of 8 by conjugation.

This same decomposition ( $H^+$  transfer to a transition state followed by conjugation, see Fig. 4, bottom) can also be used to examine the origin of the regioselectivity.  $H^+$  transfer in position C7 is slightly more energetic than in positions C9 and C11, but the difference is less than 6 kcal mol<sup>-1</sup>. In contrast, strong differences can be observed in the conjugation term: conjugation

Table 5Energies (kcal mol<sup>-1</sup>) for the proton transfer sequence (seeFig. 4, bottom for description, compound 9 deprotonated in position 3is used as a transfer reference in all cases) of 8 in positions 7, 9 and 11

	C7	С9	C11
H <sup>+</sup> transfer	+19.8	+16.0	+15.1
Conjugation	+55.5	+39.5	+34.1
Overall transfer	-35.7	-23.5	-19.0

in position C7 is much stronger than in position C9 or C11, thus leading to the experimentally observed thermodynamic preference for position C7.

In summary, a neutral ( $\eta^{5}$ -1,2,4,5-tetramethylcyclohexadienyl)-Mn(CO)<sub>3</sub> complex 7 has been prepared and characterized by X-ray crystallography. Its reactivity toward a strong base has been studied. Thus, deprotonation of 7 at a "benzylic" position using a lithiation/electrophilic quench sequence affords functionalized complexes **10–13**. The reaction is not regioselective and the experimental results can be interpreted by a kinetic deprotonation at the C9 benzylic carbon at very low temperatures whereas thermodynamic equilibration leads to major deprotonation at the C7 benzylic carbon at higher temperatures. This is confirmed and decomposed in terms of lithium binding and electron delocalization by theoretical computations on the lithiation products of compound 7.

# **Experimental section**

#### Syntheses

 $[(\eta^{6}-1,2,4,5-\text{Tetramethylbenzene})\text{Mn}(\text{CO})_{3}]^{+}\text{BF}_{4}^{-}$  complex 1.<sup>10</sup> The "silver (I) method" using  $BrMn(CO)_5$ , and  $AgBF_4^$ and the corresponding free arene was used.16 In a Schlenk tube is introduced successively AgBF<sub>4</sub> (0.973 g, 0.5 mmol), BrMn(CO)<sub>5</sub> (1.374 g, 0.5 mmol), dry freshly distilled CH<sub>2</sub>Cl<sub>2</sub>, 10 mL under Ar and the mixture is stirred for 2 h under reflux. Distilled tetramethylmethylbenzene (2.682 g, 0.5 mmol) is added and the reaction mixture stirred under reflux for 16 h. The solution is cooled and filtered on Celite and concentrated under a N<sub>2</sub> stream. It is better to avoid evaporation of all the solvents under reduced pressure because the yield decreases dramatically. The resulting solution is mixed with diethylether and the complex precipitates as a yellow powder (1.620 g, 0.45 mmol, 90% yield). IR (neat) 2058, 1994 cm<sup>-1</sup> Mn-CO. <sup>1</sup>H NMR, 200 MHz,  $C_3D_6O$ ,  $\delta$  2.54 (s, 12H, Me), 6.83 (s, 2H, ArH). <sup>13</sup>C NMR (100 MHz,  $C_3D_6O$ ):  $\delta$  17.5 (CH<sub>3</sub>), 103.5 (C3 and C6), 115.4 (C1, C2, C4, C5), 217.3 Mn(CO). HRMS (ESI, positive mode): m/z calcd for C<sub>13</sub>H<sub>14</sub>MnO<sub>3</sub><sup>+</sup>, 273.0323; found, 273.0318. Anal. calcd for C13H14MnO3BF4: C, 37.01; H, 3.34%; found: C, 36.89; H, 3.22%.

( $\eta^5$ -1,2,4,5-Tetramethylcyclohexadienyl)Mn(CO)<sub>3</sub> complex 7. [( $\eta^6$ -1,2,4,5-Tetramethylmethylbenzene)Mn(CO)<sub>3</sub>]<sup>+</sup>BF<sub>4</sub><sup>--</sup> complex 1 (0.360 g, 1 mmol) in dry THF (10 mL) treated with an excess of LiAlH<sub>4</sub> (19 mg, 0.5 mmol) at -78 °C afforded a yellow solution which was stirred for 2 h. HCl (1 M, 1 mL) is added and the reaction mixture was treated with Et<sub>2</sub>O (20 mL). The organic phase is poured into a saturated NaCl aqueous solution (20 mL) and the resulting organic phase dried over MgSO<sub>4</sub>. The solvent was removed under reduced pressure and purified on 15–40 µm silica gel with petroleum ether, PE, which yields the ( $\eta^5$ -tetramethylcyclohexadienyl)Mn(CO)<sub>3</sub> complex 7 (182 mg) in 66% yield. IR (neat) 1997, 1901 cm<sup>-1</sup> Mn–CO. <sup>1</sup>H NMR, 200 MHz, CdCl<sub>3</sub>,  $\delta$  1.58 (s, 6H, Me<sup>7</sup>, Me<sup>8</sup>), 1.85 (s, 6H, Me<sup>9</sup>, Me<sup>10</sup>), 2.41 (d, J = 13 Hz, 1H, H<sup>6exo</sup>), 2.51 (d, J = 13 Hz, 1H, H<sup>6endo</sup>), 5.43 (s, 1H, H<sup>3</sup>). Anal. calcd for C<sub>13</sub>H<sub>15</sub>MnO<sub>3</sub>: C, 56.94; H, 5.51%; found: C, 56.78; H, 5.34%.

(η<sup>5</sup>-1-Trimethylsilylmethyl-2,4,5-trimethylcyclohexadienyl)- $Mn(CO)_3$  and  $(n^5-2$ -trimethylsilylmethyl-1,4,5-trimethylcyclohexadienyl)Mn(CO)<sub>3</sub> complexes 10 and 11.  $(\eta^{5}-1,2,4,5-Tetra$ methylcyclohexadienyl)Mn(CO)3 complex 7 (0.274 g, 1 mmol) is dissolved in freshly distilled dry THF (10 mL). Distilled TMEDA (4 equiv.) is added and the solution cooled down at -78 °C. n-BuLi (1.6 M in hexane, 4 equiv.) is added slowly and the reaction mixture stirred for 2 h at -40 °C. Then an excess of ClSiMe<sub>3</sub> is added (0.434 g, 4 equiv.) and the reaction mixture is stirred for 2 h at -40 °C and then at rt for 2 h. Then water is added. In this flask, Et<sub>2</sub>O is poured and the organic phase recovered and washed with a saturated aqueous NaCl solution and dried over MgSO4. The solvent is removed under reduced pressure and the crude material purified by a silica gel chromatography column. Using a 9:1 mixture of PE/Et<sub>2</sub>O we eluted complexes 10 and 11 in 73% yield in the ratio 3:1, 0.253 g. HRMS (ESI, positive mode): m/z $369.0689 \text{ M} + \text{Na}^+$ , calcd for  $C_{16}H_{23}MnO_3SiNa$ : 369.0695. Anal. calcd: C, 55.48; H, 6.69%; found: C, 55.32; H, 6.49%. IR (neat)  $\nu$  (cm<sup>-1</sup>): 1996, 1898 [Mn(CO<sub>3</sub>)]. Complex 10 <sup>1</sup>H NMR (200 MHz, CdCl<sub>3</sub>): δ 0.00 (s, 9H, SiMe<sub>3</sub>), 1.55 (m, 8H, CH<sub>2</sub>, Me<sup>9</sup> and Me<sup>10</sup>), 1.85 (s, 3H, Me<sup>8</sup>), 2.42 (d, J = 13 Hz, 1H,  $H^{6exo}$ ), 2.52 (d, J = 13 Hz, 1H,  $H^{6endo}$ ), 5.41 (s, 1H,  $H^{3}$ ). Complex 11 <sup>1</sup>H NMR (200 MHz, CdCl<sub>3</sub>):  $\delta$  0.11 (s, 9H, SiMe<sub>3</sub>), 1.55 (m, 8H, CH<sub>2</sub>, Me<sup>7</sup> and Me<sup>8</sup>), 1.80 (s, 3H, Me<sup>10</sup>), 2.40 (d, J = 13 Hz, 1H, H<sup>6exo</sup>), 2.50 (d, J = 13 Hz, 1H, H<sup>6endo</sup>), 5.27 (s, 1H, H<sup>3</sup>).

 $(\eta^{5}-1-Diphenylphosphinomethyl-2,4,5-trimethylcyclohexadie$ nyl)Mn(CO)<sub>3</sub> and  $(\eta^{5}-1,4,5-trimethyl-2-diphenylphosphino$ methylcyclohexadienyl)Mn(CO)<sub>3</sub> complexes 12 and 13. ( $\eta^5$ -1,2,4,5-Tetramethylcyclohexadienyl)Mn(CO)<sub>3</sub> complex 7 (0.274 g, 1 mmol) is dissolved in freshly distilled dry THF (10 mL). Distilled TMEDA (4 equiv.) is added and the solution cooled down at -78 °C. n-BuLi (1.6 M in hexane, 4 equiv.) is added slowly and the reaction mixture stirred for 2 h at -40 °C. Then an excess of ClPPh<sub>2</sub> is added (2.20 g, 10 equiv.) and the reaction mixture stirred for 2 h at -40 °C and then at rt for 2 h. Then water is added. In this flask, Et<sub>2</sub>O is poured and the organic phase recovered and washed with a saturated aqueous NaCl solution and dried over MgSO<sub>4</sub>. The solvent is removed under reduced pressure and the crude material purified by a silica gel chromatography column. Using a mixture of PE/Et<sub>2</sub>O in the ratio 9:1 we eluted complexes 12 and 13 in 82% yield in the ratio 3:1, 0.376 g. HRMS (ESI, positive mode): m/z 481.0737 M + Na<sup>+</sup>, calcd for C25H24MnO3PNa: 481.0741. Anal. calcd: C, 55.48; H, 6.69%; found: C, 55.32; H, 6.49%. IR (neat)  $\nu$  (cm<sup>-1</sup>): 1998, 1905 [Mn(CO<sub>3</sub>)]. Complex 12 <sup>1</sup>H NMR (200 MHz, CdCl<sub>3</sub>): δ 1.49 (s, 3H, Me<sup>8</sup>), 1.54 (s, 3H, Me<sup>10</sup>), 1.83 (s, 3H, Me<sup>9</sup>), 2.45  $(d, J = 13 \text{ Hz}, 1\text{H}, \text{H}^{6\text{exo}}), 2.55 (d, J = 13 \text{ Hz}, 1\text{H}, \text{H}^{6\text{endo}}),$ 2.70 (d, J = 12 Hz, 1H, H<sup>7</sup>), 2.90 (d, J = 12 Hz, 1H, H<sup>7</sup>), 5.35 (s, 1H, H<sup>3</sup>), 7.45 (m, 10H, PPh<sub>2</sub>). Complex **13** <sup>1</sup>H NMR (200 MHz, CdCl<sub>3</sub>):  $\delta$  1.28 (s, 3H, Me<sup>7</sup>), 1.29 (s, 3H, Me<sup>8</sup>), 1.74 (s, 3H, Me<sup>10</sup>), 2.43 (d, J = 13 Hz, 1H, H<sup>6exo</sup>), 2.53 (d, J = 13 Hz, 1H, H<sup>6endo</sup>), 2.80 (d, J = 12 Hz, 1H, H<sup>9</sup>), 2.87 (d, J = 12 Hz, 1H, H<sup>9</sup>), 5.10 (s, 1H, H<sup>3</sup>), 7.45 (m, 10H, PPh<sub>2</sub>).

# **Computational details**

Full geometry optimizations were systematically conducted with no symmetry constraints using the Gaussian 03 program<sup>17</sup> within the framework of the Density Functional Theory (DFT) using the hybrid B3LYP exchange-correlation functional<sup>18</sup> and the 6-31+G(d,p) basis set for all atoms including Mn as implemented in the Gaussian program. Frequencies were evaluated within the harmonic approximation and used unscaled to confirm the nature of all minima (no complex frequency and fulfilment of the criteria on the forces) having two H atoms on C6 (frequencies for compounds derived from 3 with a phenyl group at C6 were not computed). For key structures, importance of adding an implicit solvation was examined using single point computations on gas phase optimized geometry. For these computations, the PCM model using the dielectric constant implemented for THF ( $\varepsilon_{\rm R} = 7.58$ ) and the default implemented in Gaussian 03 are used.<sup>19</sup>

# Acknowledgements

We thank CNRS for financial support, Hélène Rousselière for the determination of the X-ray structures, Centre de Résolution de Structures, IPCM, UMR 7201 and Noémie Elgrishi for a preliminary study.

# References

- (a) M. F. Semmelhack, J. H. T. Hall, R. Farina, M. Yoshifuji, G. Clark, T. Bargar, K. Hirotsu and J. Clardy, J. Am. Chem. Soc., 1979, 101, 3535; (b) M. F. Semmelhack, in Comprehensive Organometallic Chemistry II, ed. G. Wilkinson, E. W. Abel and F. G. A. Stone, Pergamon Press, Oxford, UK, 1995, vol. 2.4, p. 517; (c) A. Fretzen, A. Ripa, R. Liu, G. Bernardinelli and E. P. Kündig, Chem.-Eur. J., 1998, 4, 251; (d) F. Rose-Munch and E. Rose, in Modern Arene Chemistry, ed. D. Astruc, Wiley-VCH, 2002, ch. 11, p. 368; (f) M. Rosillo, G. Dominguez and J. Pérez-Castells, Chem. Soc. Rev., 2007, 36, 1589; (g) D. Astruc, Organometallic Chemistry and Catalysis, Springer, Heidelberg, 2007, p. 243.
- 2 (a) K. F. McDaniel, in Comprehensive Organometallic Chemistry II, ed. E. W. Abel, F. G. A. Stone and G. Wilkinson, Pergamon Press, Oxford, 1995, vol. 6, p. 93; (b) A. R. Pape, K. P. Kaliappan and E. P. Kündig, Chem. Rev., 2000, 100, 2917; (c) F. Rose-Munch and E. Rose, Eur. J. Inorg. Chem., 2002, 1269; (d) D. Prim, B. Andrioletti, F. Rose-Munch, E. Rose and F. Couty, Tetrahedron, 2004, 60, 3325; (e) D. A. Sweigart, J. A. Reingold and S. U. Son, in Comprehensive Organometallic Chemistry, ed. R. H. Crabtree and D. M. P. Mingos, Elsevier, Oxford, 2006, 3rd edn, vol. 5, ch. 10, pp. 761–814; (f) F. Rose-Munch, E. Rose and A. Eloi, in Cationic (η<sup>6</sup>-arene)-and neutral (η<sup>5</sup>-cyclohexadienyl)-tricarbonylmanganese complexes: Synthesis and reactivity. Patai's Chemistry of Functional Groups, ed. Marek and Rappoport, The Chemistry of Organomanganese Compounds, 2011, pp. 489–558; (g) F. Rose-Munch and E. Rose, Org. Biomol. Chem., 2011, 9, 4725.
- 3 (*a*) D. Astruc, *Tetrahedron*, 1983, **39**, 4027; (*b*) J. C. Boutonnet and E. Rose, *J. Organomet. Chem.*, 1981, **221**, 157.
- 4 J. P. Djukic, F. Rose-Munch, E. Rose and Y. Dromzee, J. Am. Chem. Soc., 1993, 115, 6434.

- (a) J. C. Boutonnet, F. Rose-Munch, E. Rose, Y. Jeannin and F. Robert, J. Organomet. Chem., 1985, 297, 185;
  (b) J. C. Boutonnet, F. Rose-Munch and E. Rose, Tetrahedron Lett., 1985, 26, 3989;
  (c) F. Rose-Munch, E. Rose and A. Semra, J. Chem. Soc., Chem. Commun., 1986, 1551;
  (d) F. Rose-Munch, E. Rose and A. Semra, J. Chem. Soc., Chem. Commun., 1987, 942;
  (e) J. C. Boutonnet, F. Rose-Munch, E. Rose and A. Semra, Bull. Soc. Chim. Fr., 1987, 640;
  (f) F. Rose-Munch, E. Rose, A. Semra and C. Bois, J. Organomet. Chem., 1989, 363, 103;
  (g) F. Rose-Munch, E. Rose, A. Semra, J. Garcia-Oricain and C. Knobler, J. Organomet. Chem., 1989, 363, 297;
  (h) F. Rose-Munch, K. Aniss, E. Rose and J. Vaisserman, J. Organomet. Chem., 1991, 415, 223;
  (i) J. P. Djukic, F. Rose-Munch, E. Rose, F. Simon and Y. Dromzee, Organometallics, 1995, 14, 2027.
- (a) F. Balssa, V. Gagliardini, F. Rose-Munch and E. Rose, Organometallics, 1996, 15, 4373; (b) A. Auffrant, D. Prim, F. Rose-Munch, E. Rose, S. Schouteeten and J. Vaissermann, Organometallics, 2003, 22, 1898; (c) B. Jacques, M. Chavarot, F. Rose-Munch and E. Rose, Angew. Chem., Int. Ed., 2006, 45, 3481; (d) B. Jacques, A. Chanaewa, M. Chavarot-Kerlidou, F. Rose-Munch, E. Rose and H. Gérard, Organometallics, 2008, 27, 626; (e) A. Eloi, F. Rose-Munch and E. Rose, J. Am. Chem. Soc., 2009, 131, 14178; (f) F. Rose-Munch, A. Marti, D. Cetiner, J. P. Tranchier and E. Rose, Dalton Trans., 2011, 40, 1567.
- (a) J. W. Johnson and P. M. Treichel, J. Chem. Soc., Chem. Commun., 1976, 688; (b) P. M. Treichel and J. W. Johnson, Inorg. Chem., 1977, 16, 749; (c) P. M. Treichel, K. P. Fivizzani and K. J. Haller, Organometallics, 1982, 1, 931; (d) R. J. Bernhardt and D. P. Eyman, Organometallics, 1984, 3, 1445; (e) R. J. Bernhardt, M. A. Wilmoth, J. J. Weers, D. M. LaBrush and D. P. Eyman, Organometallics, 1986, 5, 883; (f) D. M. LaBrush, D. P. Eyman, N. C. Baenziger and L. M. Mallis, Organometallics, 1991, 10, 1026; (g) J. W. Hull, K. J. Roesselet and W. L. Gladfelter, Organometallics, 1992, 11, 3630.
- 8 (a) G. Jaouen, Ann. N. Y. Acad. Sci., 1977, 295, 59; (b) S. G. Davies, S. J. Coote and C. L. Goodfellow, in Advances in Metal Organic Chemistry, ed. L. S. Liebeskind, JAI Press, Greenwich, 1991, vol. 2, pp. 1–57; (c) S. G. Davies and T. D. McCarthy, in Comprehensive Organometallic Chemistry II, ed. E. W. Abel, F. G. A. Stone and G. Wilkinson, Pergamon Press, Oxford, UK, 1995, vol. 12, pp. 1039–1070; (d) T. Volk, D. Bernicke, J. W. Bats and H.-G. Schmalz, Eur. J. Inorg. Chem., 1998, 1883.
- 9 (a) D. Astruc, E. Roman, J. R. Hamon and P. Batail, J. Am. Chem. Soc., 1979, 101, 2240; (b) J. R. Hamon, D. Astruc, E. Roman, P. Batail and J. J. Mayerle, J. Am. Chem. Soc., 1981, 103, 2431; (c) D. Astruc, J. R. Hamon, E. Roman and P. Michaud, J. Am. Chem. Soc., 1981, 103, 7502; (d) C. M. Casado, T. Wagner and D. Astruc, J. Organomet. Chem., 1995, 502, 143; (e) H. A. Trujillo, C. M. Casado, J. Ruiz and D. Astruc, J. Am. Chem. Soc., 1999, 121, 5674; (f) D. Astruc, Acc. Chem. Res., 2000, 33, 287.
- 10 J. Dubarle-Offner, F. Rose-Munch, E. Rose, N. Elgrishi and H. Rouselière, Organometallics, 2010, 29, 4643.
- 11 J. D. Jackson, S. J. Villa, D. S. Bacon, R. D. Pike and G. B. Carpenter, Organometallics, 1994, 13, 3972.
- 12 For theoretical justification of the negative charge at the Mn(CO)<sub>3</sub> centre, see (a) R. Hoffmann and P. Hofmann, J. Am. Chem. Soc., 1976, **98**, 598; (b) O. Eisenstein, W. M. Butler and A. J. Pearson, Organometallics, 1984, **3**, 1150.
- 13 An identical feature is observed for the isoelectronic chromium complex: C. A. Merlic, M. M. Miller, B. N. Hietbrink and K. N. Houk, J. Am. Chem. Soc., 2001, **123**, 4909.
- (a) A. Pfletschinger, T. K. Dargel, J. W. Bats, H.-G. Schmalz and W. Koch, *Chem.-Eur. J.*, 1999, 5, 537; (b) C. A. Merlic, J. C. Walsh, D. J. Tantillo and K. N. Houk, *J. Am. Chem. Soc.*, 1999, 121, 3596.
- 15 I. Chataigner, C. Panel, H. Gérard and S. R. Piettre, Chem. Commun., 2007, 3288.
- 16 A. J. Pearson and I. C. Richards, J. Organomet. Chem., 1981, 204, C25.
- 17 M. J. Frisch et al., Gaussian 03, Revision C.02, Gaussian Inc., Wallingford CT, 2004.
- 18 (a) C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B*, 1988, **37**, 785; (b) B. Miehlich, A. Savin, H. Stoll and H. Preuss, *Chem. Phys. Lett.*, 1989, **157**, 200; (c) A. D. J. Becke, *Chem. Phys.*, 1993, **98**, 5648.
- 19 M. Cossi, G. Scalmani, N. Rega and V. Barone, J. Chem. Phys., 2002, 117, 43 and references therein.