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A Novel Order of *ortho*-Directing Abilities in the Lithiation of η^6-Arenetricarbonylchromium(0) Complexes

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Abstract: A ranking order of *ortho*-lithiation directed by various functional groups in arenetricarbonylchromium complexes has been determined. This order differs from that found in the free arene series. Inductive effects were found to be the dominant factor for the determination of the site of lithiation. Fluorine was found the most powerful *ortho* director of the groups studied. Additionally, fluorine was found to be a strong *ortho* director in the uncomplexed series under kinetic conditions.

The regiocontrolled polyfunctionalisation of aromatic compounds is an important goal in synthesis and one of the most powerful techniques for achieving this is directed lithiation. The ability of a substituent to direct lithiation to an *ortho* site has been much studied[1] and a general ranking order of directing ability has been determined by competition studies[2]. This is an extensive list but a set of examples pertinent to this paper are:—

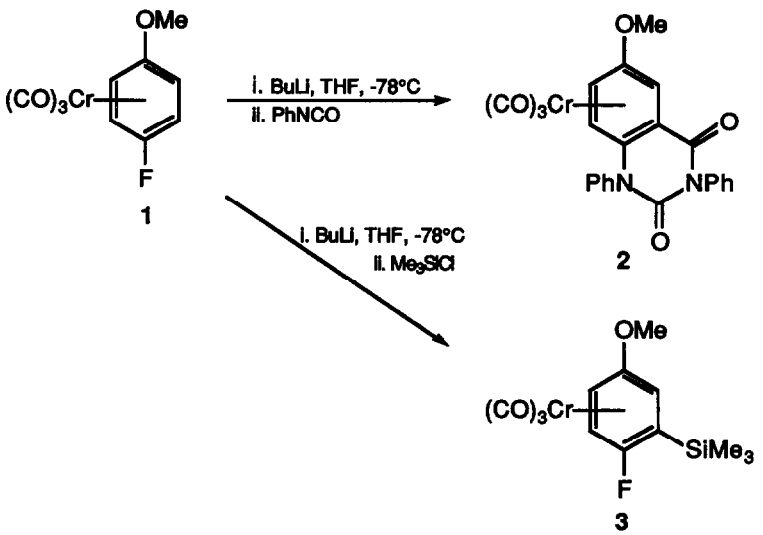
$$-CONR_2 > -CO_2NHR > -NHCOR > -CH_2NR_2 > -OMe > -NMe_2 \sim -F$$

However, since the precise reaction conditions can markedly influence the site of metallation, the above order requires careful interpretation[2e,3].

The kinetic acidities of the aromatic protons expressed in directed lithiations have been interpreted in terms of two main properties of the functional group: labilisation of the *ortho* proton by electron withdrawal and coordination of the incoming base[1]. It is the balance of these factors,

which is changed by complexation of the arene to chromium, which will be the concern of this report.

The enhancement of acidity of the ring protons on coordination of an arene to the tricarbonylchromium unit, makes deprotonation at low temperatures a facile process[4]. The regioselectivity of lithiation in monosubstituted arene complexes has been studied by Card and Trahanovsky[4b], who noted the strong *ortho* directing effects of the fluoro and methoxy groups. In a preliminary communication, we reported the reversal of normal regiocontrol in lithiation of fluoroanisole complexes[5a], and the use of these systems in synthesis[6]. The regiochemistry of lithiation of these disubstituted complexes was determined by a combination of chemical transformation and nmr analysis[5a] and the 1,4- case is shown in Scheme 1.



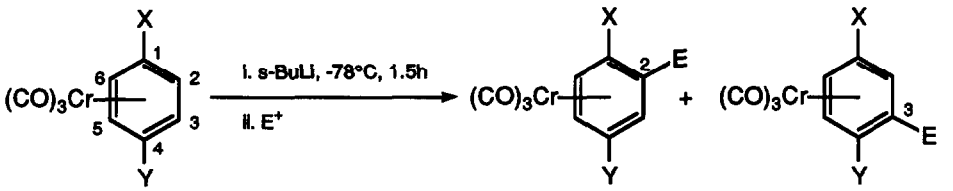
Scheme 1

Thus complex (1) was lithiated (BuLi, THF, –78°C, 1h) and the lithio- species quenched with phenyl isocyanate (2 equiv) to generate the quinoxaline complex (2)[7]. Alternatively, the lithio-intermediate was quenched with chlorotrimethylsilane to give a product which was shown by n.O.e. studies[5a] to be (3). In a control experiment, a 1:1·08 mixture of anisoletricarbonyl-chromium(0) and fluorobenzenetricarbonylchromium(0) were lithiated with 0·9 equivalents of butyl lithium and the product quenched with chlorotrimethylsilane. 2-Trimethylsilylfluorobenzene complex was isolated in 93 % yield (based on BuLi) and the residual products were shown by nmr analysis to contain the equivalent of a 2–3 % yield of 2-trimethylsilylanisole. The inherent dominance of a fluoro- substituent was thus demonstrated unambiguously.

The X-ray analysis of the solid state structures of (1)[5a] and related compounds revealed that the methoxy group of (1) was almost in the plane of the aryl ring and that, whilst the C–F bond length

(1.351Å) was comparable that in uncomplexed aryl fluorides (1.35Å)[5b], that of the aryl C–O bond of (1) (and comparable aryl ether complexes[5c]) was slightly shortened (1.346Å, *cf* uncomplexed aryl methyl ethers, ≈1.36Å[5d]). This indicates enhanced double bond character to the C–O bond and hence enhanced positive character to the oxygen atom. The effect would be to diminish the coordinative directing ability of the group. Directing ability would now be dominated by the inductive effect and in this the fluorine is the more powerful[8]. This phenomenon is more pronounced in the nitrogen series where typically a bond shortening of ≈0.06Å is obseved upon complexation[5c,e].

We sought to extend the study to other *ortho* directing functional groups to see whether their relative abilities were enhanced or reduced on complexation of the arene and whether the above explanation was generally applicable. Intramolecular competitive lithiations were carried out on a series of 1,4-disubstituted arene complexes (Scheme 2) which were prepared by standard methods[9].



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E^+ = Me_3SiCl unless stated otherwise.

X = -NMe_2, -CH_2NMe_2, -CH_2OMe, -NHCO^{t}Bu, -OMe, -CONHPh.

Y = -F, -OMe

Scheme 2

The results are summarised in the Table. The position of electrophilic quenching and the proportions of regioisomers obtained, where appropriate, are shown. In each case, results for the complexed system are compared to those for the free arene; where data was not available, control experiments were carried out under identical conditions.

As found previously by this group[5,7] and others[10], different regiocontrol does indeed operate in lithiations of disubstituted arenetricarbonylchromium(0) complexes compared with the free arenes. As proposed above, we deem inductive electron withdrawal to be the most important factor in determining site of lithiation[11]. Coordinative directing groups such as dimethylaminomethyl were found to be less effective in competition with electron withdrawing groups in the complexed series than in the free arenes. For example, in the absence of *N,N,N',N'*-tetramethylethylenediamine, 4-methoxy-*N,N*-dimethylbenzylamine is reported to lithiate exclusively adjacent to the alkylamino function[2b] (conditions: BuLi / 27°C / 20h), in contrast to the complexed arene where the methoxy

group exhibits comparable directing power.

Table: Isolated Yields (%) of Products (2) and (3).

	Y \ X	-CH_2NMe_2	-CH_2OMe	-$NHCO^tBu$[a]	-OMe	-CONHPh
COMPLEXES	-F	0 / 83	0 / 61[c]	7[d] / 65	0 / 93	57
	-OMe	34 / 31		51 / 18		
ARENES	-F	0[e] / 80	54[f] / 30	12 / 0[g]	40 / 37	
	-OMe	80[h] / 0		38[i] / 18		

[a] Reagents: i, 2-3 eq. BuLi; ii, MeI; iii, hv / air. Yields are for decomplexed arenes.

[b] X and Y are *ortho* to each other in the starting complex. Reagents: i, LDA, 2 equiv; ii, Me_3SiCl. Also obtained was starting material (19 %) and the product of fluoride displacement by diisopropylamine (11 %).

[c] Starting material recovered (10 %).

[d] Yields based on isolated arene and ^1H nmr / g.l.c.. analysis of mixed flash chromatography fractions. In addition the 3,5-bismethyl derivative was obtained (7 %).

[e] Lithiation under the conditions shown in the Scheme, gave substitution *ortho* to fluorine only, equilibration of the lithiated intermediate at –78°C for 3h gave a 10:1 mixture of the 3- and 2- silylated arenes respectively, combined yield by g.l.c. analysis,75 %.

[f] Yields by g.l.c. analysis, only α-metallation with no Wittig rearrangement was observed.

[g] Significant aryl deprotonation only occurred above 0°C (the dianion does not form at lower temperatures) and leads to benzyne formation[12] and complex product mixtures which were not isolated. The low yield of 2-substituted arene implies that the major site of lithiation is *ortho* to fluorine.

[h] Ref. 2b; reagents: i, BuLi / 27°C / 24h; ii, Ph_2CO.

[i] Ref. 13; reagents: i, 3 equiv. BuLi / 25°C / 20h; ii, $(MeS)_2$. The 2,5-bisthiomethyl derivative (18 %) was also obtained.

When in competition with a secondary carboxamido group which directs predominantly by strong coordination, the methoxy function proved to be slightly less efficient and the dominance of the pivalamido (dimethylpropionamido) group as an *ortho*-director was reinforced in relation to

the uncomplexed case. More useful were the results of lithiation of the *para* fluoroarene complexes. Substitution occurred exclusively *ortho* to fluorine in all cases except that of the 4-fluoropivalanilide complex, where 7 % substitution *ortho* to the amide function was observed in addition to formation of the bis-methylated derivative where both positions *ortho* to fluorine had reacted.

Attempts to prepare 4-fluorobenzamide complex by direct or indirect means were unsuccessful, so that a competition between $-CONR_2$ and fluorine was only possible for the 1,2-disubstituted complex prepared from *o*-lithiofluorobenzene complex and one equivalent of phenyl isocyanate. In this case the non-nucleophilic base LDA was used since butyl lithium reagents favoured displacement of fluoride over deprotonation of this very electron deficient system[14]. For the same reasons, it was not feasible to prepare and lithiate complexes containing other powerfully electron withdrawing groups such as $-SO_2NR_2$ or 2-oxazoline; fluoroarenes containing the latter group undergo nucleophilic displacement by butyl lithium even without coordination to chromium[15].

That these changes in regioselectivity observed on complexation were attributable to the influence of $Cr(CO)_3$, and not simply a consequence of low temperature kinetic control, was established by our experiments on the free fluoroarenes. There has been some controversy over the major site of lithiation of 4-fluoroanisole, initially reported by Slocum[2b] to be exclusively *ortho* to the methoxy group, although other workers[16] had noted the formation of both regioisomers. Our result of a 55:45 ratio (by g.l.c., conditions: s-BuLi, 1.5h at –78°C) of the 2- and 3-substituted arenes respectively is in agreement with that recently reported by Kirk *et al*[3] who found evidence of equilibration under these conditions to the thermodynamically favoured lithio-chelate *ortho* to methoxy group.

In the control lithiation of 4-fluoro-*N,N*-dimethylbenzylamine, carried out in the light of the fluoroanisole result, substitution was observed predominantly *ortho* to fluorine (up to 80 % yield), however in some runs small amounts of the second regioisomer were observed by g.l.c. and nmr analysis. The literature reports functionalisation *ortho* to the alkylamino group only[1]; although no experimental details are given. We thought it likely that equilibration between kinetic and thermodynamic *o*-lithio species occurs for this system as in the fluoroanisole case[3]. To test this, the lithioarene was stirred at –78°C for 3h before being quenched with chlorotrimethylsilane. G.l.c. analysis of the product mixture revealed a 10:1 ratio of regioisomers with the minor (thermodynamic product) substituted *ortho* to the $-CH_2NMe_2$ function.

The group $-CH_2OMe$ was included for completeness although not a good *ortho* director in the uncomplexed series due to preferential benzylic deprotonation, often followed by a Wittig rearrangement[17]. Studies by Blagg and Davies[18] have demonstrated benzylic lithiation without rearrangement in the tricarbonylchromium complexes. Subsequent lithiation of the α-functionalised benzyl methyl ether complex occurred *ortho* to the -CHXOMe group[18]. However, no substitution *ortho* to the $-CH_2OMe$ group was observed by us on lithiation of 4-fluorobenzyl

methyl ether complex, only *ortho* to fluorine. Lithiation of the uncomplexed arene gave a 60:40 product mixture in favour of benzylic substitution. Surprisingly, no Wittig rearranged product was observed in this experiment, presumably due to the low temperature employed and stabilisation of the benzylic anion by the *para* fluoro group.

We can now construct the following order of *ortho*-directing abilities of functional groups in arenetricarbonylchromium complexes:

$$\text{-F} > \text{(-CONHR)} > \text{-NHCOR} > \text{-CH}_2\text{NR}_2 \approx \text{-OMe} >> \text{-CH}_2\text{OMe}$$

Under the stated conditions, the relative kinetic acidity of a ring proton takes precedence over simple base coordination by a heteroatom in the substituent group as the principal factor in determining the site of metallation in disubstituted arene complexes. In lithiations of these complexes, high yields and the clean products obtained, coupled with the high regioselectivity found for the fluoro systems, and the easy displacement of fluoride by nucleophiles[6,19] make the functionalisation of aromatic substrates in this way very attractive. In addition to its mechanistic interest, this new directing order allows the prediction of alternative regiochemistries which can be invaluable for strategies of polysubstituted aromatic compound synthesis.

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EXPERIMENTAL

Melting points were carried out on a Kofler hot stage and are uncorrected; infrared spectra were recorded on Perkin Elmer 1700 FT spectrometer; ^{1}H nmr on a Perkin Elmer R32 (90 MHz), Bruker WH-250 FT (250 MHz), or Jeol GSX FT (270 MHz) spectrometers, the latter with a GSX data system. Gas chromatographs were recorded on Varian Vista 6000 chromatograph with a chromosorb WHP 80–100 mesh column (OV 101), with a Varian Vista CDS 401 data system.

All reactions involving complexes or butyl lithium were carried out under an atmosphere of dry, oxygen free nitrogen. Unless otherwise stated, petrol refers to petroleum ether b.p. 60–80°C.

Reductive *N*-dimethylation of the benzylamines was carried out by the method of Borch[20]. So prepared were 4-methoxy-*N,N*-dimethylbenzylamine as a colourless oil (1.59 g; 53 %), which was obtained pure by bulb to bulb distillation, oven temperature 125°C, 70 mmHg (1.26 g; 42 %), and *4-fluoro*-N,N-*dimethylbenzylamine* which was purified by bulb to bulb distillation, oven temperature 125°C, 76 mmHg, (1.23 g, 50 %) as a colourless oil; ν_{max} (film) 2945, 2817, 2770, 1603, 1509, 1458, 1223, 1017, 857 and 818 cm^{-1}; δ_H ($CDCl_3$, 90 MHz) 2.20 (6H, s), 3.38 (2H, s), 7.00 (2H, t, *J* 8.0 Hz), 7.25 (2H, d, *J* 8.0 Hz); *m/z* 153 (M^+), 136, 109 (100 %), 83, 58. (Found: C,

70.65; H, 7.94; N, 9.37. $C_9H_{12}FN$ requires: C, 70.56; H, 7.90; N, 9.14 %).

The pivalanilides were prepared by the method of Fuhrer and Gschwend[13] in a two phase mixture of aqueous sodium carbonate and dichloromethane. So prepared were 4-methoxypivalanilide (90 %), m.p. 126°C (lit.[13] m.p. 125°C) and *4-fluoropivalanilide*, as colourless needles (91 %) m.p. 126°C; ν_{max} (Nujol) 3283, 2876, 1650, 1537, 1511, 1407, 1227 and 1212 cm^{-1}; δ_H ($CDCl_3$, 90 MHz) 1.28 (9H, s), 6.96 (2H, t, *J* 8.0 Hz), 7.43 (2H, dd, *J* 8.0, 5.0 Hz); *m/z* 195 (*M*+), 152, 137, 111, 57 (100 %). (Found: C, 67.44; H, 7.17; N, 7.08. $C_{11}H_{14}FNO$ requires: C, 67.6; H, 7.23; N, 7.17 %).

4-Fluorobenzyl methyl ether. — 4-Fluorobenzyl alcohol (3.58 g, 28.4 mmol) in THF (25 ml), was added to sodium hydride (60 % w/v dispersion in mineral oil, 1.36 g, 34 mmol) under nitrogen, and the mixture stirred at 50°C for 4 h. To the cooled suspension at 0°C was added methyl iodide (4.82 g; 2.12 ml; 34 mmol) in THF (10 ml). The reaction mixture was stirred at room temperature for 16 h. Diethyl ether was added and the suspension filtered through Celite; solvents were removed to leave a colourless oil. The pure *compound* (3.20 g, 80 %) was obtained by bulb to bulb distillation at 50 mmHg, oven temperature 85°C; ν_{max} (film) 2928, 2823, 1605, 1510, 1224, 1098 and 825 cm^{-1}; δ_H ($CDCl_3$, 90 MHz) 3.40 (3H, s), 4.41 (2H, s), 7.00 (2H, t, *J* 8.0 Hz), 7.28 (2H, dd, *J* 8.0, 5.0 Hz); *m/z* 140 (*M*+), 139, 123, 121, 109 (100 %), 107. (Found: C, 68.51; H, 6.76. C_8H_9FO requires: C, 68.56; H, 6.47 %).

General Procedure for the Preparation of (η^6-Arene)tricarbonylchromium(0) Complexes.

The arene and chromium hexacarbonyl in di-n-butyl ether – THF mixtures, were heated to reflux under nitrogen in a Strõhmeier apparatus[21] for the stated times. The reaction mixtures were cooled and filtered through a Celite pad, and solvents removed to leave the crude products. The pure complexes were obtained by column chromatography and recrystallisation as necessary.

(η^6-4-*Fluoroanisole*)*tricarbonylchromium*(0) (4, X = OMe, Y = F).— Freshly distilled 4-fluoroanisole (6.0 ml) and chromium hexacarbonyl (2.95 g, 13.4 mmol) were refluxed for 16 h. as described. After work up and crystallisation, the product was obtained as yellow needles (1.69 g, 48 %), m.p. 66.5–67.5°C (lit.[22] m.p. 69–70°C); ν_{max}.($CHCl_3$) 1985, 1895, 1480 cm^{-1}; δ_H ($CDCl_3$, 90 MHz) 3.68 (3H, s), 5.27 (2H, dd, *J* 7, 2 Hz), 5.60 (2H, dd, *J* 7, 4 Hz). (Found: C, 45.52; H, 2.57. Calc. for $C_{10}H_7CrFO_4$: C, 45.81; H, 2.69 %).

(η^6-4-*Methoxy*-N,N-*dimethylbenzylamine*)*tricarbonylchromium*(0) (4, X = CH_2NMe_2, Y = OMe)[23]. — 4-Methoxy-*N,N*-dimethylbenzylamine (1.26 g, 7.64 mmol) and chromium hexacarbonyl (1.98 g, 9.0 mmol), in di-n-butyl ether (65 ml) and THF (7.0 ml), were heated to reflux for 48 h. as described. Column chromatography (basic alumina, petrol : ether 70 : 30) and recrystallisation gave the title compound as yellow crystals (1.77 g, 77 %) m.p. 74.5–75.5°C (lit.[23] m.p. 74°C); ν_{max} (Nujol) 1970, 1953, 1861 cm^{-1}; δ_H ($CDCl_3$, 90 MHz) 2.20 (6H, s), 2.97 (2H, s), 3.62 (3H, s), 5.06 (2H, d, *J* 6.5 Hz), 5.48 (2H, d, *J* 6.5 Hz); *m/z* 301 (*M*+), 245, 217, 174, 164, 121, 95 (100 %), 52. (Found: C, 51.79; H, 4.84; N, 4.65. Calc. for $C_{13}H_{15}CrNO_4$: C, 51.83; H, 5.02; N,

4.65 %).

(η^6-4-*Fluoro*-N,N-*dimethylbenzylamine*)*tricarbonylchromium*(0) (4, X = CH_2NMe_2, Y = F). — 4-Fluoro-*N,N*-dimethylbenzylamine (0.81 g, 5.29 mmol) and chromium hexacarbonyl (1.4 g, 6.35 mmol), in di-n-butyl ether (65 ml) / THF (9 ml), were heated to reflux as described for 18 h. Column chromatography (basic alumina, petrol : ether 70 : 30) and recrystallisation gave the *title compound* (630 mg, 41 %) as yellow needles m.p. 60.5–62°C; ν_{max} (Nujol) 2933, 1985, 1967, 1913, 1833 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 2.25 (6H, s), 2.99 (2H, s), 5.33 (2H, dd, *J* 6.4, 4.5 Hz), 5.50 (2H, dd, *J* 6.4, 2.2 Hz); *m/z* 289 (*M*+), 233, 205, 152, 134, 109, 95 (100 %), 58, 52. (Found: C, 49.80; H, 4.19; N, 4.99. $C_{12}H_{12}CrFNO_3$ requires: C, 49.83; H, 4.18; N, 4.84 %).

[η^6-4-*Fluoro(methoxymethyl)benzene*]*tricarbonylchromium*(0) (4, X = CH_2OMe, Y = F). — 4-Fluoro(methoxymethyl)benzene (1.5 g, 10.7 mmol) and chromium hexacarbonyl (2.82 g, 12.8 mmol) in di-n-butyl ether (70 ml) / THF (8 ml), were heated to reflux as described for 16 h. Column chromatography (silica gel H, petrol : ether 80 : 20) gave the *title compound* (1.795 g, 61 %) as yellow needles m.p. 59–60°C; ν_{max} (CCl_4) 2928, 1986, 1919, 1481, 1227 and 1100 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 3.40 (3H, s), 3.98 (2H, s), 5.33 (2H, dd *J* 6.63, 4.75 Hz), 5.54 (2H, dd *J* 6.63, 2.81 Hz); *m/z* 276 (*M*+), 245, 220, 192, 162, 140, 121, 109, 82, 52 (100 %). (Found: C, 47.83; H, 3.26. $C_{11}H_9CrFO_4$ requires: C, 47.84; H, 3.28 %).

(η^6-4-*Fluoropivalanilide*)*tricarbonylchromium*(0) (4, X = $NHCOBu^t$, Y = F). — 4-Fluoropivalanilide (1.637 g, 8.39 mmol) and chromium hexacarbonyl (2.20 g, 10.07 mmol) in di-n-butyl ether (70 ml) and THF (12 ml), were heated to gentle reflux as described for 24 h..Column chromatography (silica gel H, petrol : ether 90 : 10 → 50 : 50) gave the starting arene (1.271 g, 78 %), followed by the *title complex* (209 mg, 7.5 %) m.p. 99–100°C (dec.); ν_{max} (CCl_4) 2965, 1984, 1918, 1704, 1540 and 1482 cm^{-1}; δ_H ($CDCl_3$, 270 MHz) 1.26 (9H, s), 5.56 (2H, dd *J* 8.0, 6.0 Hz), 5.91 (2H, dd *J* 8.0, 3.0 Hz), 6.76 (1H); *m/z* 331 (*M*+), 303, 275, 247 (100 %), 195, 162, 122, 111, 71, 57, 52. (Found: C, 50.57; H, 4.2; N, 4.23. $C_{14}H_{14}CrFNO_4$ requires: C, 50.76; H, 4.26; N, 4.23 %).

(η^6-4-*Methoxypivalanilide*)*tricarbonylchromium*(0) (4, X = $NHCOBu^t$, Y = OMe). — Chromium hexacarbonyl (2.26 g, 10.3 mmol) in acetonitrile was heated to reflux for 24 h. The orange solution was cooled to room temperature and solvent evaporated, to leave trisacetonitriletricarbonylchromium[24] as a pale yellow solid. To the complex was added; by catheter, under nitrogen, 4-methoxypivalanilide (1.00 g, 4.83 mmol) in THF (50 ml). The reaction mixture was kept at ≈ 60°C for 12 h. Workup as described for the other complexes, followed by column chromatography (silica gel H, dry flash column, eluant petrol : ether 50 : 50 → 100 : 0) gave the *title compound* (1.195 g, 72 %) as fine yellow needles m.p. 88–90°C; ν_{max} (CCl_4) 3452, 2967, 1972, 1902, 1698, 1499, 1438 and 1253 cm^{-1}; δ_H ($CDCl_3$, 90 MHz) 1.21 (9H, s), 3.62 (3H, s), 5.23 (2H, d *J* 7.0 Hz), 5.89 (2H, d *J* 7.0 Hz), 6.72 (1H); *m/z* 343 (*M*+), 287, 259, 207, 123, 108, 57 (100 %). (Found: C, 52.44; H, 5.03; N, 4.18. $C_{15}H_{17}CrNO_5$ requires: C, 52.48; H, 4.99; N, 4.08 %).

(η⁶-N-*Phenyl*-2-*fluorobenzamide*)*tricarbonylchromium*(0) (6, X = H, Y = F, E = CONHPh). — This was prepared as previously described[7], m.p. 134–135 °C (lit.[7] m.p. 126.5–128°C), spectroscopically identical to the earlier material.

General Procedure for Lithiations.

The complex in THF (≈ 25 ml per mmol), at –78°C, was treated with n-butyl lithium (1.0 equiv) and the solution stirred at this temperature for the stated time. Unless otherwise stated, chlorotrimethylsilane (excess) was added and the solution allowed to warm to room temperature overnight. The product mixture was poured into aqueous ammonium chloride* (15 % w/v) / ether, and the ether portion separated, washed with water, dried, and the solvents evaporated. Metal complexes were isolated by column chromatography, and recrystallisation (dichloromethane / petrol) as necessary, to give analytically pure material. For the free arenes, the product mixtures were analysed by g.l.c.; products were separated and purified by column chromatography, vacuum distillation, or recrystallisation as appropriate.

*For basic amines, the reaction mixtures were poured into distilled water / ether; and the aqueous portion basified (2M NaOH) before separation of the organic layer.

Lithiation of (η⁶-Arene)tricarbonylchromium(0) *Complexes.*

(η⁶-4-*Fluoroanisole*)*tricarbonylchromium*(0) (1) — The complex (1) (214 mg, 0.82 mmol) was lithiated for 45 min. After column chromatography (silica gel H, petrol : ether 85 : 15), the *product* (6, X = OMe, Y = F, E = $SiMe_3$) (254 mg, 93 %) was isolated as yellow crystals, m.p. 69–70°C; ν_{max} ($CHCl_3$) 1975, 1895, 1450 and 1425 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.40 (9H, s), 3.62 (3H, s), 5.22 (1H, t, *J* 2.5 Hz), 5.34 (1H, dd, *J* 7.1, 4.2 Hz), 5.45 (1H, dt, *J* 7.1, 2.5 Hz). (Found: C, 46.56; H, 4.47. $C_{13}H_{15}CrFO_4$ requires C, 46.70; H, 4.52 %).

(η⁶-4-*Fluoro*-N,N-*dimethylaniline*)*tricarbonylchromium*(0) (4, X = NMe_2, Y = F) — The complex (4, X = NMe_2, Y = F) (172 mg, 0.62 mmol) was lithiated for 60 min. Column chromatography (silica gel H, petrol : ether 99 : 1) gave two complexes, in order of elution: [η⁶-3,5-*bis*(*trimethylsilyl*)-4-*fluoro*-N,N-*dimethylaniline*]*tricarbonylchromium*(0), m.p. 135–136°C; ν_{max} ($CHCl_3$) 1957 and 1875 cm^{-1}; δ_H ($CDCl_3$, 90 MHz) 0.35 (18H, s), 2.69 (6H, s), 5.14 (2H, d, *J* 2.5 Hz); *m/z* 419 (*M*⁺), 363, 335, 283; (Found: *M*⁺, *m/z* 419.0847. $C_{17}H_{26}CrFNO_3Si_2$ requires *M*⁺, 419.0840); the *complex* (6, X = NMe_2, Y = F, E = $SiMe_3$), (166 mg, 0.48 mmol, 77 %), isolated as yellow crystals, m.p. 75.5–76.5°C; ν_{max}·($CHCl_3$) 1960, 1880, 1530 and 860 cm^{-1}; δ_H ($CDCl_3$, 90 MHz) 0.38 (9H, s), 2.75 (6H, s), 4.81 (1H, t, *J* 2.5 Hz), 5.16 (1H, dt, *J* 7.0, 2.5 Hz), 5.39 (1H, dd, *J* 7.0, 4.0 Hz). (Found: C, 48.53; H, 5.09; N, 4.08. $C_{14}H_{18}CrFNO_3Si$ requires C, 48.41; H, 5.22; N, 4.03 %).

(η⁶-4-*Methoxy*-N,N-*dimethylbenzylamine*)*tricarbonylchromium*(0) (4, X = CH_2NMe_2, Y = OMe). — The complex (4, X = CH_2NMe_2, Y = OMe) (200 mg, 0.66 mmol) was lithiated for 1.5 h.

Column chromatography (silica gel H, petrol : ether 95 : 5 → 5 : 95) gave, in order of elution: (η^6-4-*methoxy*-2-*trimethylsilyl*-N,N-*dimethylbenzylamine*)*tricarbonylchromium*(0) (5, X = CH_2NMe_2, Y = OMe, E = $SiMe_3$) as yellow crystals (84 mg, 34 %) m.p. 65–67°C; ν_{max} (Nujol) 1967, 1955, 1873, 1528 and 1251 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.35 (9H, s), 2.18 (6H, s), 2.64 and 3.41 (2H, AB quartet, *J* 12.5 Hz), 3.66 (3H, s), 5.19 (1H, d, *J* 2.3 Hz), 5.24 (1H, dd, *J* 6.8, 2.3 Hz), 5.44 (1H, d, *J* 6.8 Hz); *m/z* 373 (M^+), 317, 289, 246 (100 %), 95, 52; (Found: C, 51.17; H, 6.23; N, 3.59. $C_{16}H_{23}CrNO_4Si$ requires: C, 51.46; H, 6.21; N, 3.75 %) and (η^6-4-*methoxy*-3-*trimethylsilyl*-N,N-*dimethylbenzylamine*)*tricarbonylchromium*(0) (6, X = CH_2NMe_2, Y = OMe, E = $SiMe_3$) as yellow crystals (77 mg, 31 %) m.p. 75–76°C; ν_{max} (Nujol) 1968, 1950, 1895 and 1257 cm^{-1}; δ_H ($CDCl_3$, 270 MHz) 0.32 (9H, s), 2.25 (6H, s), 2.95 (2H, AB quartet, *J* 12.7 Hz), 3.70 (3H, s), 4.97 (1H, d, *J* 7.0 Hz), 5.57 (1H, d, *J* 1.7 Hz), 5.71 (1H, dd, *J* 7.0, 1.7 Hz); *m/z* 373 (M^+), 317, 289 (100 %), 246, 193, 95, 52. (Found: C, 51.72; H, 6.34; N, 3.64. $C_{16}H_{23}CrNO_4Si$ requires: C, 51.46; H, 6.21; N, 3.75 %).

(η^6-4-*Fluoro*-N,N-*dimethylbenzylamine*)*tricarbonylchromium*(0) (4, X = CH_2NMe_2, Y = F). — The complex (4, X = CH_2NMe_2, Y = F) (174 mg, 0.60 mmol) was lithiated for 1.5 h. Basic workup as described above, and column chromatography (basic alumina, petrol : ether 70 : 30) gave a single product: (η^6-4-*fluoro*-3-*trimethylsilyl*-N,N-*dimethylbenzylamine*)*tricarbonylchromium* (0) (6, X = CH_2NMe_2, Y = F, E = $SiMe_3$) as a yellow oil, (181 mg, 83 %); ν_{max} (CCl_4) 2953, 2822, 1980, 1913, 1441 and 1255 cm^{-1}; δ_H ($CDCl_3$, 270 MHz) 0.39 (9H, d, *J* 1.0 Hz), 2.25 (6H, s), 2.94 (2H, s), 5.26 (1H, dd, *J* 7.0, 4.9 Hz), 5.48 (1H, dd, *J* 3.0, 1.9 Hz), 5.66 (1H, ddd, *J* 7.0, 3.0, 1.9 Hz); *m/z* 361 (M^+), 305, 277, 234, 224, 206, 95 (100 %). (Found: C, 50.07; H, 5.89; N, 3.65. $C_{15}H_{20}CrFNO_3Si$ requires: C, 49.85; H, 5.58; N, 3.88 %).

[η^6-4-*Fluoro(methoxymethyl)benzene*]*tricarbonylchromium*(0) (4, X = CH_2OMe, Y = F). — The complex (4, X = CH_2OMe, Y = F) (150 mg, 0.54 mmol) was lithiated for 1.5 h. Column chromatography (silica gel H, petrol : ether 90 : 10), gave [η^6-4-*fluoro*-3-*trimethylsilyl*(*methoxymethylbenzene*)]*tricarbonylchromium*(0) (6, X = CH_2OMe, Y = F, E = $SiMe_3$) as a yellow oil (115 mg, 61 %); ν_{max} (CCl_4) 2820, 1981, 1916, 1440 and 1255 cm^{-1}; δ_H ($CDCl_3$, 270 MHz) 0.37 (9H, d, *J* 1.0 Hz), 3.41(3H, s), 3.94 (2H, s), 5.26 (1H, dd, *J* 6.9, 4.9 Hz), 5.51 (1H, dd, *J* 2.8, 1.8 Hz), 5.68 (1H, ddd, *J* 6.9, 2.8, 1.8 Hz); *m/z* 348 (M^+), 292, 264, 234, 193, 52 (100 %); (Found: C, 48.45; H, 4.9 requires: C, 48.27; H, 4.92 %) and returned starting material (15 mg, 10 %).

(η^6-4-*Methoxypivalanilide*)*tricarbonylchromium*(0) (4, X = $NHCOBu^t$, Y = OMe). — The complex (4, X = $NHCOBu^t$, Y = OMe) (291 mg, 0.85 mmol) was treated with 3 equivalents of n-butyl lithium for 1.5h. Methyl iodide (0.15 ml, ≈2 equiv) was added, and the reaction allowed to warm to room temperature overnight. The crude yellow product mixture was dissolved in dichloromethane, and exposed to air and sunlight until the solution became colourless. The solution was filtered through Celite and evaporated to leave a colourless oil. Column chromatography (silica gel H, petrol : ether 90 : 10 → 80 : 20) gave, in order of elution: 4-*methoxy*-3-*methylpivalanilide* as

colourless needles (from dichloromethane / petrol) (33 mg, 18 %) m.p. 112–114°C; ν_{max} (CCl_4) 3461, 2960, 1685, 1505, 1466 and 1235 cm^{-1}; δ_H ($CDCl_3$ 250 MHz) 1.30 (9H, s), 2.20 (3H, s), 3.80 (3H, s), 6.75 (1H, d, *J* 8.5 Hz), 7.19 (1H, br.s), 7.27 (1H, d, *J* 2.5 Hz), 7.31 (1H, dd, *J* 8.5, 2.5 Hz); *m/z* 221 (*M*+), 178, 138, 137, 136, 122, 57 (100 %); (Found: C, 70.31; H, 8.73; N, 6.36. $C_{13}H_{19}NO_2$ requires: C, 70.56; H, 8.65; N, 6.33 %); *4-methoxy-2-methylpivalanilide* (recrystallised: dichloromethane / petrol) as colourless cubic crystals (96 mg, 51 %) m.p. 95–96°C; ν_{max} (CCl_4) 3420, 2960, 1687, 1514, 1422, 1284 and 1221 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.30 (9H, s), 2.20 (3H, s), 3.78 (3H, s), 6.73 (1H, dd, *J* 9.37, 3.1 Hz), 6.73 (1H, d, *J* 3.1 Hz), 7.09 (1H, br.s), 7.53 (1H, d, *J* 9.4 Hz); *m/z* 221 (*M*+), 163, 138, 137, 136, 122, 57 (100 %). (Found: C, 70.28; H, 8.79; N, 6.20. $C_{13}H_{19}NO_2$ requires: C, 70.56; H, 8.65; N, 6.33 %).

(η^6-*4-Fluoropivalanilide*)*tricarbonylchromium*(0) (4, X = NHCOBu^t, Y = F). — The complex (4, X = NHCOBu^t, Y = F) (189 mg, 0.57 mmol) was treated with 2.2 equivalents of n-butyl lithium for 2 h. Methyl iodide (0.1 ml, ≈ 2 equivalents) was added and the reaction allowed to warm to room temperature overnight. Work up and decomplexation as above gave the product mixture as a yellow oil (215 mg) which was decomplexed as above to give the product mixture as colourless crystals. Column chromatography (silica gel H, petrol : ether 90 : 10 → 80 : 20) gave *4-fluoro-3,5-dimethylpivalanilide* (9 mg, 7 %) as colourless needles (recrystallised dichloromethane / petrol) m.p. : sublimes >130 °C; ν_{max} (CCl_4) 3462, 2961, 2860, 1730, 1288 and 1219 cm^{-1}; δ_H ($CDCl_3$, 270 MHz) 1.30 (9H, s), 2.23 (6H, d, *J* 2.2 Hz), 7.17 (2H, d, *J* 6.1 Hz); *m/z* 223 (*M*+), 139, 57 (100 %). (Found: C, 70.10, H, 8.14, N, 6.28. $C_{13}H_{18}FNO$ requires: C, 69.93, H, 8.13, N, 6.27 %); *4-fluoro-3-methylpivalanilide* (70 mg, 59 %) as fine colourless needles (recrystallised dichloromethane / petrol) m.p. 109–110°C; ν_{max} (CCl_4) 3460, 2976, 2869, 1743, 1692, 1524, 1501, 1214 and 1118 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.29 (9H, s), 2.21 (3H, d, *J* 1.7 Hz), 6.91 (1H, t, *J* 9.0 Hz), 7.21 (2H, m), 7.40 (1H, dd, *J* 6.9, 2.7 Hz); *m/z* 209 (*M*+), 125, 85, 57 (100 %). (Found: C, 68.70, H, 7.88, N, 6.54. $C_{12}H_{16}FNO$ requires: C, 68.88, H, 7.71, N, 6.69 %). The third eluted band contained a mixture of the compound described above and *4-fluoro-2-methylpivalanilide* (23 mg), which could not be separated; the yields / ratio were determined by g.l.c. (35 and 38 % respectively), and nmr (~ 1 : 1). The 2-methyl derivative was identical in all respects to the lithiation product obtained from the non complexed arene *vide infra.*

(η^6-N-*Phenyl-2-fluorobenzamide*)*tricarbonylchromium*(0) — (η^6-*N*-Phenyl-2-fluorobenzamide)tricarbonylchromium(0) was dissolved in THF (30 ml) and treated with LDA (2 equivalents) for 60 min followed by chlorotrimethylsilane (0.5 ml, excess) as before. After column chromatography (SiO_2, petrol : ether 90 : 10), (η^6-N-*phenyl-2-fluoro-3-trimethylsilylbenzamide*)*tricarbonylchromium*(0) (119 mg, 57 %) was isolated as orange crystals, m.p. 178–180°C; ν_{max}.($CHCl_3$) 3460, 1992, 1930, 1680, 1602, 1525, 1360, 1130 and 845 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.43 (9H, d, *J* 1.5 Hz), 4.95 (1H, td, *J* 6.3, 3.4 Hz), 5.64 (1H, ddd, *J* 6.3, 2.6, 1.5 Hz), 7.18 (1H, t, *J* 7.5 Hz), 7.38 (2H, t, *J* 7.5 Hz), 7.61(2H, d, *J* 7.5 Hz), 8.09 (1H, d, *J* 13.5

Hz); *m/z* 423 (*M*+), 367, 339, 287. (Found: C, 54.16, H, 4.24, N, 3.37. $C_{19}H_{18}CrFNO_4Si$ requires C, 53.89, H, 4.28, N, 3.31 %). The second eluted compound was (η^6-2-*di*(1-*methylethyl*)*amino*-N-*phenylbenzamide*)*tricarbonylchromium*(0) (22.5 mg, 11 %), orange crystals, m.p. 106–108°C; $\nu_{max.}$($CHCl_3$) 3380, 1980, 1908, 1670, 1601, 1538, 1314 and 1105 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.30 (6H, d, *J* 6.9 Hz), 1.36 (6H, d, *J* 6.9 Hz), 3.72 (2H, sept, *J* 6.9 Hz), 5.23 (1H, d, *J* 6.1 Hz), 5.29 (1H, t, *J* 6.1 Hz), 5.58 (1H, dd, *J* 6.1, 1.5 Hz), 6.36 (1H, dd, *J* 6.1, 1.5 Hz), 7.14 (1H, t, *J* 7.8 Hz, H4'), 7.37 (2H, t, *J* 7.8 Hz), 7.65 (2H, d, *J* 7.8 Hz), 11.05 (1H, s); *m/z* 432 (*M*+), 376, 348, 304. (Found: C, 61.32, H, 5.36, N, 6.59. $C_{22}H_{24}CrN_2$ requires: C, 61.11, H, 5.59, N, 6.48 %). In addition, starting material (19 %) was recovered.

Control Lithiation of Arenes.

Lithiation of 4-*fluoro*-N,N-*dimethylbenzylamine.* — The arene (193 mg, 1.27 mmol) in THF (35 ml) was cooled to –78°C and treated with s-butyl lithium (1.1 equivalents) for 1.5 h. Chlorotrimethylsilane (0.75 ml, excess) was added and the solution allowed to warm to room temperature overnight. The product mixture was obtained as a pale yellow oil, g.l.c. analysis showed one silylated product and starting material in the ratio: 83 : 13. Column chromatography (basic alumina, petrol : ether 90 : 10) gave 4-*fluoro*-3-*trimethylsilyl*-N,N-*dimethylbenzylamine* as a colourless oil (180 mg; 80 %); ν_{max} (film) 2954, 2901, 2859, 2817, 1473, 1457, 1251, 1204, 1077 and 842 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.30 (9H, d, *J* 0.8 Hz), 2.21 (6H, s), 3.35 (2H, s), 6.90 (1H, t, *J* 8.6 Hz), 7.25 (2H, m); *m/z* 225 (*M*+), 224, 181, 167, 165, 152, 58 (100 %). (Found: C, 64.07, H, 9.16, N, 6.23. $C_{12}H_{20}FNSi$ requires: C, 63.95, H, 8.94, N, 6.21 %). The arene (92 mg; 0.6 mmol) was treated as above with s-butyl lithium at –78°C for 3h. Work-up as described gave the product mixture as a pale yellow oil, containing starting material, the 3-silylated and 2- silylated benzylamines in the ratios: 13:78:8 by g.l.c. Column chromatography (SiO_2, petrol:ether 95 : 5 to 100 % ether) gave 4-*fluoro*-2-*trimethylsilyl*-N,N-*dimethylbenzylamine* as a colourless oil (9 mg; ~7 %); ν_{max} (film) 2927, 2857, 2818, 2771, 1575, 1252, 1217 and 840 cm^{-1}; δ_H ($CDCl_3$, 270 MHz) 0.30 (9H, s), 2.18 (6H, s), 3.44 (2H, s), 6.97 (1H, td, *J* 8.5, 2.8 Hz), 7.18 (1H, dd, *J* 9.7, 2.8 Hz), 7.38 (1H, dd, *J* 8.5, 5.5 Hz); *m/z* 225 (*M*+) 210 (100 %), 194, 181, 167, 109, 85, 84, 49. (Found: *M*+ 225.1343; $C_{12}H_{20}FNSi$ requires 225.1349) and the 3-silylated compound (70 mg; 52 %) as described above.

4-*Fluoro*(*methoxymethyl*)*benzene.* — The arene (171 mg, 1.22 mmol) was treated as in the general procedure and the solution allowed to warm to room temperature over 3 h. The product mixture was obtained as a colourless oil (242 mg) product yields by g.l.c., 59 and 36 %. Column chromatography (silica gel H, petrol : ether 100 : 0 → 90 : 10) gave: 4-*fluoro*-α-(*trimethylsilyl*) *benzyl methyl ether* as a colourless oil (55 % based on g.l.c.); ν_{max} (CCl_4) 2960, 2861, 1605, 1506, 1249, 1224, 1096, 874 and 846 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) -0.03 (9H, s), 3.33 (3H, s), 3.90 (1H, s), 6.95 (2H, t, *J* 9.2 Hz), 7.09 (2H, dd, *J* 9.2, 6.0 Hz); *m/z* 211 (*M*+–1), 197, 169, 139, 120,

73 (100 %) (Found: C, 62.36, H, 8.26. $C_{11}H_{17}FOSi$ requires: C, 62.22, H, 8.07 %); 4-*fluoro*-3-(*trimethylsilyl)benzyl methyl ether* as a colourless oil (33 % based on g.l.c.); ν_{max} (CCl_4) 2958, 2816, 1474, 1251, 1209, 1100, 1077 and 844 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.29 (9H, d, *J* 0.9 Hz), 3.38 (3H, s), 4.39 (2H, s), 6.94 (1H, t, *J* 8.1 Hz), 7.30 (2H, m); *m/z* 212 (M^+), 197, 181, 163, 165 (100 %), 139, 45. (Found: C, 62.10, H, 8.14. $C_{11}H_{17}FOSi$ requires: C, 62.22, H, 8.07 %).

4-*Fluoropivalanilide.* — The arene (276 mg, 1.41 mmol) in THF (35 ml), was cooled to 0°C and treated with n-butyl lithium (2.2 equivalents) for 3.5 h. Methyl iodide (0.1 ml) was added and the mixture allowed to warm to room temperature overnight. Work up gave the crude product as a pale yellow oil, g.l.c. analysis showed the starting arene and one methylated derivative as the only volatile substances in a complex mixture of products (tlc, silica petrol : ether 70 : 30). The major product: 4-*fluoro*-2-*methylpivalanilide*, was isolated by column chromatography (silica gel H, petrol : ether 90 : 10) as colourless cubic crystals(35 mg, 12 %) recrystallised dichloromethane / petrol m.p. 95–96°C; ν_{max} (CCl_4) 3477, 2963, 1690, 1512, 1205 and 1150 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.31 (9H, s), 2.21 (3H, s), 6.88 (2H, m), 7.10 (1H, bs), 7.65 (1H, dd, *J* 9.2, 5.0 Hz); *m/z* 209 (M^+), 125, 85, 57 (100 %). (Found: C, 68.82, H, 7.82, N, 6.74. $C_{12}H_{16}FNO$ requires: C, 68.88, H, 7.71, N, 6.69 %).

4-*Fluoroanisole.* — The arene (450 mg, 3.57 mmol) was treated as in the general procedure Work up gave the product mixture as a colourless oil (637 mg). Column chromatography (silica gel H, petrol : ether 95 : 5) gave: 4-*fluoro*-2-*trimethylsilylanisole* (51 % based on g.l.c.), distilled bulb to bulb at 9 mmHg, oven temperature 90°C (lit.[16] b.p. 62–64°C at 2 mmHg.); ν_{max} (film) 2956, 2900, 2841, 1604, 1478, 1395, 1261, 1241, 1202 and 841 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.25 (9H, s), 3.77 (3H, s), 6.72 (1H, dd, *J* 8.8, 3.8 Hz), 6.95 (1H, ddd, *J* 8.8, 8.00, 3.1 Hz), 7.03 (1H, dd, *J* 8.00, 3.1 Hz); *m/z* 198 (M^+), 183, 153 (100 %), 125, 109 (Found: C, 60.31, H, 7.83. Calc. for $C_{10}H_{15}FO$: C, 60.57, H, 7.62 %); 4-*fluoro*-3-*trimethylsilylanisole* (38 % based on g.l.c.) distilled bulb to bulb at 7 mmHg, oven temperature 70°C; ν_{max} (film) 2957, 2902, 2836, 1581, 1474, 1262, 1250, 1200, 1041, 887 and 842 cm^{-1}; δ_H ($CDCl_3$, 270 MHz) 0.32 (9H, d, *J* 1.0 Hz), 3.79 (3H, s), 6.84 (1H, ddd, *J* 8.6, 4.4, 3.2 Hz), 6.90 (1H, dd, *J* 3.9, 3.2 Hz), 6.92 (1H, dd, *J* 8.6, 7.4 Hz); *m/z* 198 (M^+), 183, 168, 153, 125, 121 (100 %), 105. (Found: C, 60.45 H, 7.86. $C_{10}H_{15}FO$ requires: C, 60.57 H, 7.62 %).

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