Synthesis of Substituted Phenyl Ketones via Pd-Catalysed Hydrodechlorination of Their Polychlorinated Derivatives

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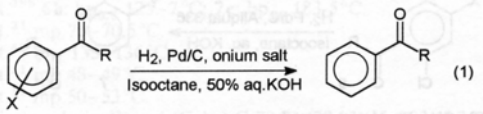
The following compounds, 2- and 3-methylacetophenones, 2- and 3-methylbenzophenones, and 2,2′-, 2,3′- and 3,3′-dimethylbenzophenones have been synthesized through a Pd-catalysed hydrodechlorination of the corresponding dichlorinated derivatives. The reaction has been carried out under multiphase conditions at 30–50 °C, by bubbling H_2 at atmospheric pressure into a biphasic system constituted by an organic substrate solution (isooctane solvent) and an aqueous alkaline solution (50% aq KOH), in the presence of Pd/C (5% wt) and Aliquat 336 (tricaprylylmethylammonium chloride). Likewise, fluorinated aceto- and benzophenones (4-fluoro-3-methylacetophenone and 4-fluoro-3-methylbenzo-, 4-fluoro-2′,3-dimethylbenzo-, 4-fluoro-3,3′-dimethylbenzophenones) have been prepared starting from the corresponding chlorinated methylfluoro- and dimethylfluoro ketones. Under such conditions, the presence of the onium salt allows the reaction to proceed with a high chemoselectivity: chlorine is removed while both the reduction of the carbonyl group and/or fluorine removal are prevented.

By far the most important procedure for the preparation of aryl ketones is the Friedel–Crafts (F.C.) acylation of aromatic hydrocarbons, because of its wide applicability and the relatively mild conditions involved.[1–3] Nevertheless, it is well known that when aromatics with activating substituents are the reagents, the acylation is not regioselective: mixtures of *ortho*- and *para*-substituted ketones are obtained, and no *meta* derivatives (or only traces) can be prepared. This difficulty could be overcome if easily removable protecting groups are properly placed as substituents in the aromatic ring of the reagents.

The question can be approached by utilizing halo substituents as the protecting groups to be removed by selective hydrodehalogenation reactions. We recently reported that, operating at 30–50 °C in a biphasic system constituted by an organic apolar solvent and an aqueous alkaline solution (KOH aq 50%), in the presence of 5% Pd/C and a quaternary onium salt, polychlorinated aromatics were rapidly hydrodechlorinated to the corresponding aromatic hydrocarbons; H_2 was introduced at atmospheric pressure.[4–6] When chlorofluoro aromatics were reacted, the reactions selectively yielded the corresponding fluorohydrocarbons in substantially quantitative yields. Also, under such conditions, the hydrodehalogenation of some halogenated aromatic ketones proceeded with a high chemoselectivity: that is, halides removal occurred without any reduction of the carbonyl group (Eq. 1),[9] whereas under classical conditions (ethanol solvent), both the hydrogenation of the carbonyl functionality and hydrodehalogenation take place simultaneously.[7,8]



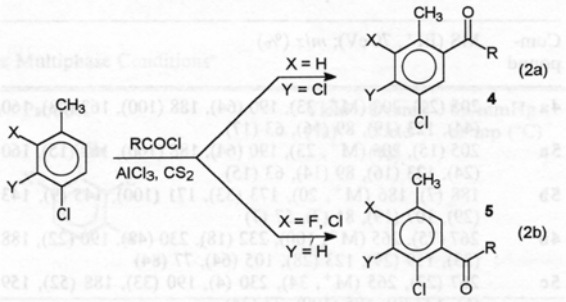
(1)

X = Cl, Br; R = CH_3, CH_2CH_3, Ph

These results prompted us to investigate the synthetic potential of the multiphase hydrodechlorination reaction for the preparation of aryl ketones otherwise difficult to synthesize via a direct electrophilic acylation.

Here, we focus our attention on the synthesis of methyl and fluoromethyl aceto- and benzophenones, with methyl substituents in *ortho*- and *meta*-positions. Chlorinated toluenes or fluorotoluenes were firstly acylated and then chlorine substituents were selectively removed under multiphase conditions (Eq. 1).

Friedel–Crafts Acylations. 3,4-Dichloro- **(1)**, 2,4-dichloro- **(2)**, and 4-chloro-2-fluorotoluene **(3)** were chosen as the substrates and they were acylated with acetyl, benzoyl, *o*-tolyl, and *m*-tolyl chlorides, respectively. According to procedures already reported for halo- and dihaloaromatics,[10–12] the F.C. reactions on compounds **1–3** were performed in carbon disulfide (Eqs. 2a–b). The results are shown in Table 1.



Although reactions 2a and 2b follow the conventional F.C. reaction scheme, very few data are reported for dihalotoluenes **(1–3)**.[13–15] In accordance with these, the results in Table 1 indicate that 3,4-dichlorotoluene **(1)** yields the corresponding 4,5-dichloro-2-methyl ketones **(4)** (*ortho*-attack with respect to the methyl group; Eq. 2b, entries 1, 4, and 6, Table 1), while 2,4-dihalotoluenes **(2–3)** yield the corresponding 2,4-dihalo-5-methylaryl ketones **(5)** (*meta*-attack with respect to the methyl group; Eq. 2a, entries 2–3, 5, and 7–11, Table 1).

Halo substituents act both as protecting (by blocking otherwise reactive ring positions) and directing groups, as reported for the acylation of both monohalotoluenes and dihalobenzenes;[1,10] compounds **4** and **5** are obtained selectively in 88–96% yields (structures are confirmed by NMR and MS).

Only the reaction of **1** with *o*-tolyl chloride (entry 6, Table 1) gives a mixture of two isomeric ketones, namely the 4,5-dichloro-2,2′-dimethyl- and the 5,6-dichloro-2,2′-dimethylbenzophenones (**4c** and **4c′**, in a 2:1 molar ratio,

Table 1. Friedel–Crafts Acylations of Dihalotoluenes[a]

Entry	Substrate	Reaction Time (h)	Product[b] (%)	Conv'n[b] (%)	Yield[c] (%)	bp/mmHg or mp (°C)
1	**1**: X = H, Y = Cl	24	**4a**: R = CH_3 (92)	100	90	108–110/1.5
2	**2**: X = Cl, Y = H	18	**5a**: R = CH_3 (92)	98	90	83–84/0.4
3	**3**: X = F, Y = H	18	**5b**: R = CH_3 (99)	100	96	69–70/0.5
4	**1**: X = H, Y = Cl	192	**4b**: R = C_6H_5 (88)	95	88	99–101
5	**2**: X = Cl, Y = H	72	**5c**: R = C_6H_5 (92)	94	89	72–74[d]
6	**1**: X = H, Y = Cl	300	**4c**: R = *o*-$CH_3C_6H_4$[e]	94	88[e]	57–60
7	**2**: X = Cl, Y = H	240	**5d**: R = *o*-$CH_3C_6H_4$ (95)	98	92	62–64
8	**2**: X = Cl, Y = H	96	**5e**: R = *m*-$CH_3C_6H_4$ (91)	94	89	59–61
9	**3**: X = F, Y = H	30	**5f**: R = C_6H_5 (96)	97	93	128–130/0.3
10	**3**: X = F, Y = H	84	**5g**: R = *o*-$CH_3C_6H_4$ (91)	94	88	79–81
11	**3**: X = F, Y = H	30	**5h**: R = *m*-$CH_3C_6H_4$ (95)	96	92	56–58

[a] All reactions were carried out using $AlCl_3$ as the catalyst in refluxing CS_2; substrate, acylating agent, and catalyst were used in a 1 : 1.2 : 1.1 molar ratio, respectively.
[b] By GC analyses.
[c] Yields are based on distilled or recrystallized products.
[d] Lit.[13] mp 78 °C.
[e] A mixture of **4c** and its isomer 5,6-dichloro-2,2′-dimethylbenzophenone (**4c′**) (in a 2 : 1 molar ratio, respectively) was isolated; the yield (88%) corresponds to that mixture.

Table 2. MS Data for Compounds **4a–c** and **5a–h**

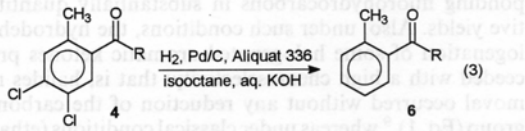
Compound	MS (EI$^+$, 70 eV); *m/z* (%)
4a	205 (21), 203 (M^+, 33), 190 (64), 188 (100), 162 (28), 160 (44), 123 (19), 89 (16), 63 (17)
5a	205 (15), 203 (M^+, 23), 190 (64), 188 (100), 162 (15), 160 (24), 123 (16), 89 (14), 63 (15)
5b	188 (7), 186 (M^+, 20), 173 (33), 171 (100), 145 (9), 143 (29), 107 (19), 81 (7), 57 (7)
4b	267 (75), 265 (M^+, 100), 232 (18), 230 (48), 190 (22), 188 (33), 159 (29), 123 (28), 105 (64), 77 (84)
5c	267 (22), 265 (M^+, 34), 230 (4), 190 (33), 188 (52), 159 (6), 123 (9), 105 (100), 77 (34)
4c	281 (3), 279 (M^+, 5), 266 (14), 264 (25), 228 (19), 159 (20), 123 (32), 119 (85), 91 (100), 65 (58)
5d	281 (5), 279 (M^+, 8), 266 (64), 264 (100), 244 (39), 208 (46), 187 (20), 119 (40), 91 (35), 65 (15)
5e	281 (10), 279 (M^+, 15), 246 (2), 244 (7), 189 (14), 187 (22), 119 (100), 91 (30), 65 (13)
5f	250 (22), 248 (M^+, 67), 173 (32), 171 (100), 143 (17), 107 (24), 105 (89), 77 (45), 51 (16)
5g	264 (5), 262 (M^+, 16), 249 (33), 247 (100), 227 (78), 212 (48), 171 (37), 119 (43), 91 (43), 65 (22)
5h	264 (9), 262 (M^+, 26), 227 (10), 173 (15), 171 (47), 119 (100), 107 (9), 91 (30), 65 (14)

respectively; structures and relative percentage amounts were determined from NOE measurements and ^{1}H NMR spectra). However, when this mixture is reacted as such under hydrodechlorination conditions, both the isomers yield the same product (see later).

Spectroscopic properties (mass and ^{1}H NMR spectra) of compounds **4a–c** and **5a–h** are given in Tables 2 and 3.

Hydrodechlorinations. Ketones **4** and **5** were hydrodechlorinated under multiphase conditions.[9] Thus, an isooctane solution of each substrate (100 mL, 1/1.4 M) was reacted in the presence of a KOH aq solution (10 mL, 50%), the catalyst (5% Pd/C), and Aliquat 336 (tricaprylylmethylammonium chloride; 0.15 molar equiv. with respect to the substrate), (Eqs. 3–4). The results are reported in Table 4.

The chemoselectivity of reactions (3) and (4) is dramatically affected by Aliquat 336, since only in its presence do the reactions proceed selectively towards the removal of chloro substituents without any concomitant reduction of the carbonyl group. In particular, derivatives **4** yield the corresponding 2-methylaceto- and benzophenones **6** (entries 1, 4 and 6), while derivatives **5** yield 3-methyl and 4-fluoro-3-methylaceto- and benzophenones **7** (entries 2–3, 5 and 7–11).



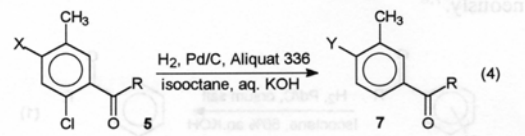


Table 3. ^{1}H NMR Data for Compounds **4a–c** and **5a–h**

Compound	^{1}H NMR ($CDCl_3$/TMS) δ, J (Hz)
4a	2.48 (s, 3H, 2-CH_3), 2.57 (s, 3H, $COCH_3$), 7.35 (s, 1H, H_3), 7.77 (s, 1H, H_6)
5a	2.37 (s, 3H, 5-CH_3), 2.64 (s, 3H, $COCH_3$), 7.43 (s, 1H, H_3), 7.46 (s, 1H, H_6)
5b	2.27 (d, 3H, 5-CH_3), 2.64 (s, 3H, $COCH_3$), 7.09 (d, 1H, H_3), 7.48 (d, 1H, H_6); $J_{CH_3,F}$ = 1.7, $J_{H_6,F}$ = 9.0, $J_{H_6,F}$ = 8.1
4b	2.28 (s, 3H, 2-CH_3), 7.39 (s, 1H, H_3), 7.48 (t, 3H, H_6, $H_{3'}$, $H_{5'}$), 7.62 (t, 1H, $H_{4'}$), 7.78 (d, 2H, $H_{2'}$, $H_{6'}$)
5c	2.38 (s, 3H, 5-CH_3), 7.45–7.50 (m, 4H, H_3, H_6, $H_{3'}$, $H_{5'}$), 7.61 (t, 1H, $H_{4'}$), 7.80 (d, 2H, $H_{2'}$, $H_{6'}$)
4c	2.36 (s, 3H, 2-CH_3), 2.46 (s, 3H, 2′-CH_3), 7.22 (tq, 1H, $H_{5'}$), 7.29 (dd, 1H, $H_{6'}$), 7.30 (dq, 1H, $H_{3'}$), 7.36 (s, 1H, H_6), 7.38 (s, 1H, H_3), 7.43 (t, 1H, $H_{4'}$); $J_{H_{3'},H_{4'}}$ = 7.2, $J_{H_{4'},H_{5'}}$ = 7.2, $J_{H_{5'},H_{6'}}$ = 7.2
4c′	2.17 (s, 3H, 2-CH_3), 2.73 (s, 3H, 2′-CH_3), 7.12 (dq, 1H, H_3), 7.19 (tq, 1H, $H_{5'}$), 7.33 (dq, 1H, $H_{6'}$), 7.34 (d, 1H, $H_{3'}$), 7.41 (d, 1H, H_4), 7.45 (t, 1H, $H_{4'}$); J_{H_3,H_4} = 8.4, $J_{H_{3'},H_{4'}}$ = 7.2, $J_{H_{4'},H_{5'}}$ = 7.2, $J_{H_{5'},H_{6'}}$ = 7.2
5d	2.37 (s, 3H, 5-CH_3), 2.56 (s, 3H, 2′-CH_3), 7.20 (t, 1H, $H_{5'}$), 7.29–7.33 (m, 3H, H_3, $H_{3'}$, $H_{6'}$), 7.42 (td, 1H, $H_{4'}$), 7.43 (s, 1H, H_6); $J_{H_{3'},H_{4'}}$ = 7.6, $J_{H_{4'},H_{5'}}$ = 7.6, $J_{H_{5'},H_{6'}}$ = 7.6
5e	2.38 (s, 3H, 5-CH_3), 2.40 (s, 3H, 3′-CH_3), 7.24 (s, 1H, H_3), 7.35 (t, 1H, $H_{5'}$), 7.42 (d, 1H, $H_{4'}$), 7.47 (s, 1H, $H_{4'}$), 7.47 (s, 1H, H_6), 7.56 (d, 1H, $H_{6'}$), 7.63 (s, 1H, $H_{2'}$); $J_{H_{4'},H_{5'}}$ = 7.6, $J_{H_{5'},H_{6'}}$ = 7.6
5f	2.28 (d, 3H, 5-CH_3), 7.14 (d, 1H, H_3), 7.24 (d, 1H, H_6), 7.47 (t, 2H, $H_{3'}$, $H_{5'}$), 7.60 (t, 1H, $H_{4'}$), 7.79 (d, 2H, $H_{2'}$, $H_{6'}$); $J_{CH_3,F}$ = 2.0, $J_{H_3,F}$ = 9.2, $J_{H_6,F}$ = 7.6, $J_{H_{2'},H3'}$ = 7.6, $J_{H_{3'},H_{4'}}$ = 7.6, $J_{H_{4'},H_{5'}}$ = 7.6, $J_{H_{5'},H_{6'}}$ = 7.6
5g	2.27 (d, 3H, 5-CH_3), 2.54 (s, 3H, 2′-CH_3), 7.11 (d, 1H, H_3), 7.20 (t, 1H, $H_{5'}$), 7.27–7.31 (m, 3H, $H_{3'}$, $H_{4'}$, $H_{6'}$), 7.40–7.46 (m, 1H, H_6); $J_{CH_3,F}$ = 2.0, $J_{H_3,F}$ = 9.2, $J_{H_6,F}$ = 7.6
5h	2.29 (d, 3H, 5-CH_3), 2.41 (s, 3H, 3′-CH_3), 7.14 (d, 1H, H_3), 7.23 (d, 1H, $H_{4'}$), 7.35 (t, 1H, $H_{5'}$), 7.42 (d, 1H, $H_{6'}$), 7.55 (d, 1H, H_6), 7.64 (s, 1H, $H_{2'}$); $J_{CH_3,F}$ = 2.0, $J_{H_3,F}$ = 8.8, $J_{H_6,F}$ = 7.6, $J_{H_{4'},H_{5'}}$ = 7.6, $J_{H_{5'},H_{6'}}$ = 7.6

Table 4. Hydrodechlorination of Dichloro- and Chlorofluoro Ketones Multiphase Conditions[a]

Entry	Substrate	Reaction Temp. (°C)	Reaction Time[b] (min)	Product	Yield[c] (%)	Overall Yield (%)	bp/mmHg or mp (°C)
1	**4a**: R = CH_3	30	240	**6a**: X = W = H; Z = COR	90	81	40–41/0.6[d]
2	**5a**: X = Cl; R = CH_3	50	135	**7a**: X = Z = H; W = COR	81	73	58–60/1.5[d]
3	**5b**: X = F; R = CH_3	50	90	**7b**: X = F; Z = H; W = COR	92	88	55–56/1.5[e]
4	**4b**: R = Ph	30	180	**6b**: X = W = H; Z = COR	76	67	138–140/0.6[f]
5	**5c**: X = Cl; R = Ph	30	270	**7c**: X = Z = H; W = COR	77	69	124–125/0.4[f]
6	**4c**: R = *o*-$CH_3C_6H_4$	30	240	**6c**: X = W = H; Z = COR	89	78	69–70[g]
7	**5d**: X = Cl; R = *o*-$CH_3C_6H_4$	30	150	**7d**: X = Z = H; W = COR	87	80	127–128/0.8[h]
8	**5e**: X = Cl; R = *m*-$CH_3C_6H_4$	30	165	**7e**: X = Z = H; W = COR	72	64	47–49[i]
9	**5f**: X = F; R = Ph	50	150	**7f**: X = F; Z = H; W = COR	88	82	52–54[j]
10	**5g**: X = F; R = *o*-$CH_3C_6H_4$	50	30	**7g**: X = F; Z = H; W = COR	91[k]	80	138–140/0.3
11	**5h**: X = F; R = *m*-$CH_3C_6H_4$	50	75	**7h**: X = F; Z = H; W = COR	90[l]	83	74–76

[a] All reactions were carried out using an isooctane solution of the substrate in the presence of aq KOH, Pd/C and Aliquat 336 (see text for details).
[b] At complete substrate conversion.
[c] Yields are based on distilled or recrystallized products.
[d] Lit.[39a] **6a**: bp_5 79°C/mmHg; **7a**: bp_{12} 109°C.
[e] Lit.[18] bp 214–215°C.
[f] Lit.[39b] **6b**: $bp_{0.3}$ 125–7°C; **7c**: bp_{16} 183-5°C.
[g] Lit.[21] mp 70–70.5°C.
[h] Lit.[40] bp_1 135–136°C.
[i] Lit.[21] mp 48–49°C.
[j] Lit.[11] mp 50–53°C.
[k] Microanalysis: Found (Calc.) C 78.71 (78.93) H 5.93 (5.74).
[l] Microanalysis: Found (Calc.) 79.08 (78.93) H 5.81 (5.74).

When no onium salt is used, a complex mixture of both halogenated and unhalogenated alcohols and hydrocarbons is obtained as already reported for the Pd-catalysed hydrodechlorinations of haloaryl ketones using methanol or ethanol as solvents.

For example, under the conditions of Table 4 but in the absence of Aliquat 336, the reaction of ketone **4c** carried out at 30 °C yields, at complete substrate conversion (8 h), a mixture of the corresponding hydrocarbon, the unhalogenated alcohol and ketone [*o*-tolylphenylmethane, α-(*o*-tolyl)benzyl alcohol, and *o*-tolylphenyl ketone] in 10, 55, and 16 % amounts (by GC), respectively, the remainder being monochlorinated alcohol (10 %) and ketone (9 %).

Table 5. MS Data for Compounds **6a–c** and **7a–h**

Compound	MS (EI$^+$, 70 eV); *m/z* (%)
6a	134 (M^+, 37), 119 (100), 91 (98), 65 (33), 51 (9)
7a	134 (M^+, 44), 119 (100), 91 (65), 65 (15), 51 (4)
7b	152 (M^+, 31), 137 (100), 19 (55), 83 (19), 63 (6), 57 (7)
6b	196 (M^+, 63), 195 (100), 178 (11), 119 (21), 105 (15), 91 (23), 77 (24), 65 (13), 51 (10)
7c	196 (M^+, 33), 181 (11), 119 (100), 105 (57), 91 (45), 77 (54), 65 (24), 51 (23)
6c	210 (M^+, 7), 209 (13), 195 (100), 177 (7), 165 (9), 119 (30), 91 (51), 65 (28)
7d	210 (M^+, 67), 209 (51), 195 (100), 177 (6), 165 (12), 119 (41), 91 (43), 65 (21)
7e	210 (M^+, 7), 195 (4), 119 (100), 91 (80), 65 (49), 51 (10)
7f	214 (M^+, 79), 199 (14), 137 (100), 109 (30), 105 (42), 83 (17), 77 (27), 51 (10)
7g	228 (M^+, 38), 227 (47), 213 (100), 137 (49), 119 (31), 109 (39), 91 (47), 83 (25), 65 (22)
7h	228 (M^+, 52), 213 (17), 137 (100), 119 (67), 109 (23), 91 (20), 83 (11), 65 (8)

The selectivity induced by the onium salt is mainly attributable to its adsorption over the catalyst,[4–5] in such a way that it actually constitutes the medium into which the reaction takes place. The onium salt may also account for different adsorption phenomena of the reagents over the catalytic surface.

As shown in Table 4, a satisfactory chemoselective dechlorination of some ketones (**4a–c**, **5c–e**, entries 1, 4, 6 and 5, 7–8, respectively) is achieved at 30 °C, although as expected, the reaction times are longer than those performed at 50 °C (entries 2–3, and 9–11).

When the reactions carried out at 30 °C on dichlorinated ketones (**4a–c** and **5c–e**) are compared (entries 1, and 4–8 of Table 4), hydrodechlorination times do not seem to be correlatable to the structures of the different halogenated compounds. Although the reacting ketones have nearly similar structures, the hydrodechlorination of **5c** requires almost twice as long as compound **5d** (entries 5 and 7); analogously, there does not seem to exist any relation between the hydrodechlorination times for compounds **4b** and **4c** and their structures (entries 4 and 6). The chlorine removal seems actually independent of the steric hindrance; at the moment the reasons for such kinetic behaviour are unclear.

As previously observed, it is noteworthy that the hydrodechlorination of the mixture of isomers **4c** and **4c′** (coming from the F.C. *o*-tolylation of 3,4-dichlorotoluene, entry 6 of Table 1) gives the 2,2′-dimethylbenzophenone as the sole product in a 89 % isolated yield (entry 6, Table 4).

In the case of chlorofluoro ketones **5b** and **5f–g** (entries 3 and 9–11), the corresponding hydrodehalogenations carried out at 50 °C, allow the selective removal of only the chloro substituents without reduction of the carbonyl group; fluoro ketones are the reaction products.[4–5]

Table 6. ^{1}H NMR for Compounds **6a–c** and **7a–h**

Compound	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)
6a	2.53 (s, 3H, 2-CH_3), 2.58 (s, 3H, $COCH_3$), 7.25 (dd, 1H, H_3), 7.27 (td, 1H, H_5), 7.38 (td, 1H, H_4), 7.70 (dd, 1H, H_6); J_{H_3,H_4} = 7.6, J_{H_4,H_5} = 7.6, J_{H_5,H_6} = 7.6, J_{H_3,H_5} = 1.2, J_{H_4,H_6} = 1.1
7a	2.41 (s, 3H, 3-CH_3), 2.59 (s, 3H, $COCH_3$), 7.33–7.39 (m, 2H, H_4, H_5), 7.74–7.78 (m, 2H, H_2H_6)
7b	2.32 (d, 3H, 3-CH_3), 2.57 (s, 3H, $COCH_3$), 7.06 (t, 1H, H_5), 7.76–7.81 (m, 1H, H_6), 7.83 (dd, 1H, H_2); $J_{CH_3,F}$ = 2.2, $J_{H_2,F}$ = 6.0, $J_{H_5,F}$ = 9.0, J_{H_5,H_6} = 8.6, J_{H_2,H_6} = 2.0
6b	2.33 (s, 3H, 2-CH_3), 7.23–7.32 (m, 3H, H_3, H_5, H_6), 7.39 (td, 1H, H_4), 7.46 (t, 2H, $H_{3'}$, $H_{5'}$), 7.59 (t, 1H, $H_{4'}$), 7.81 (d, 2H, $H_{2'}$, $H_{6'}$); J_{H_3,H_4} = 7.2, J_{H_4,H_5} = 7.2, J_{H_5,H_6} = 7.2, $J_{H_{2'},H_{3'}}$ = 7.2, $J_{H_{3'},H_{4'}}$ = 7.2, $J_{H_{4'},H_{5'}}$ = 7.2, $J_{H_{5'},H_{6'}}$ = 7.2
7c	2.42 (s, 3H, 3-CH_3), 7.34–7.41 (m, 2H, H_4, H_5), 7.48 (t, 2H, $H_{3'}$, $H_{5'}$), 7.58 (d, 2H, $H_{4'}$, H_6), 7.63 (s, 1H, H_2), 7.80 (d, 2H, $H_{2'}$, $H_{6'}$)
6c	2.44 (s, 6H, 2-,2′-CH_3), 7.20 (td, 2H, H_5), 7.28 (dd, 2H, H_3), 7.30 (dd, 2H, H_6), 7.39 (td, 2H, H_4); J_{H_3,H_4} = 7.8, J_{H_4,H_5} = 7.8, J_{H_5,H_6} = 7.8, J_{H_3,H_5} = 1.6, J_{H_4,H_6} = 1.5
7d	2.33 (s, 3H, 3-CH_3), 2.40 (s, 3H, 2′-CH_3), 7.25 (t, 1H, H_5), 7.30 (t, 2H, $H_{3'}$, $H_{5'}$), 7.34 (d, 1H, H_4), 7.37–7.41 (m, 2H, $H_{4'}$, $H_{6'}$), 7.56 (d, 1H, H_6), 7.65 (s, 1H, H_2); J_{H_4,H_5} = 6.8, J_{H_5,H_6} = 6.8 $J_{H_{3'},H_{4'}}$ = 7.6, $J_{H_{4'},H_{5'}}$ = 7.6, $J_{H_{5'},H_{6'}}$ = 7.6
7e	2.42 (s, 6H, 3-, 3′-CH_3), 7.35 (t, 2H, H_5), 7.40 (d, 2H, H_4), 7.57 (d, 2H, H_6), 7.63 (s, 2H, H_2); J_{H_4,H_5} = 7.7, J_{H_5,H_6} = 7.7
7f	2.33 (d, 3H, 3-CH_3), 7.09 (t, 1H, H_5), 7.49 (t, 2H, $H_{3'}$, $H_{5'}$), 7.59 (t, 1H, $H_{4'}$), 7.62–7.65 (m, 1H, H_6), 7.70 (dd, 1H, H_2), 7.76 (d, 2H, $H_{2'}$, $H_{6'}$); $J_{CH_3,F}$ = 2.0, $J_{H_2,F}$ = 6.0, $J_{5,F}$ = 8.8, J_{H_5,H_6} = 8.8, J_{H_2,H_6} = 2.0, $J_{H_{2'},H_{3'}}$ = 7.6, $J_{H_{3'},H_{4'}}$ = 7.6, $J_{H_{4'},H_{5'}}$ = 7.6, $J_{H_{5'},H_{6'}}$ = 7.6
7g	2.30 (d, 3H, 3-CH_3), 2.31 (s, 3H, 2′-CH_3), 7.05 (t, 1H, H_5), 7.23–7.30 (m, 3H, $H_{3'}$, $H_{5'}$, $H_{6'}$), 7.39 (td, 1H, $H_{4'}$), 7.58–7.62 (m, 1H, H_6), 7.71 (dd, 1H, H_2); $J_{CH_3,F}$ = 2.0, $J_{H_2,F}$ = 5.2, $J_{H_5,F}$ = 8.8, J_{H_5,H_6} = 8.8, J_{H_2,H_6} = 2.0
7h	2.34 (d, 3H, 3-CH_3), 2.43 (s, 3H, 3′-CH_3), 7.09 (t, 1H, H_5), 7.36 (t, 1H, $H_{5'}$), 7.41 (d, 1H, $H_{4'}$), 7.53 (d, 1H, $H_{6'}$), 7.59 (s, 1H, $H_{2'}$), 7.61–7.64 (m, 1H, H_6), 7.71 (dd, 1H, H_2); $J_{CH_3,F}$ = 2.0, $J_{H_2,F}$ = 5.6, $J_{H_5,F}$ = 8.8, J_{H_5,H_6} = 9.2, J_{H_2,H_6} = 2.0, $J_{H_{4'},H_{5'}}$ = 7.6, $J_{H_{5'},H_{6'}}$ = 7.6

Isolated yields of hydrodechlorination products **6, 7** are in the range of 72–92%; for a direct comparison with already reported syntheses (often more complicated),[11,16–36] Table 4 also indicates the overall yields (64–88%) of ketones **6, 7** prepared from the dihalogenated derivatives.

Spectroscopic properties (mass and ^{1}H NMR spectra) of compounds **6, 7** are given in Tables 5 and 6.

The two-step procedure described here provides a new strategy for a high-yield synthesis of aryl ketones otherwise difficult to prepare through a direct electrophilic acylation. In particular, the soundness of the method stands upon the proper setting up of multiphase reaction conditions which allow hydrodechlorinations of polyhalogenated ketones to proceed with a chemoselectivity towards the chlorine removal hitherto not reported. Although the role of the onium salt needs to be clarified, the procedure offers new starting points for a further development of the utilization of chloro substituents as protecting groups of aromatic derivatives.

All the compounds used were ACS grade and were employed without further purification. Melting points were determined on a Buchi 535 melting-point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian Unity 400 (400 MHz) spectrometer using $CDCl_3$ with TMS as the internal standard. *J* Values were recorded in Hz. GC analyses were performed on a Varian GC 3400CX using a fused silica capillary column (30 m × 0.25 mm) with DB5 as liquid phase (film thickness 0.25 mm). GC/MS analyses were performed on a HP 5971 mass detector at 70 eV coupled to a HP 5890-Series II gas chromatograph fitted with a 30 m × 0.25 μm, DB5 capillary column. Halogenated ketones **(4, 5)** were obtained by F.C. acylations of dihalotoluenes **(1, 3)**, according to already reported procedures.[10–13,37] The reactions were performed in CS_2 solvent by using the substrate, the appropriate acyl chloride and the catalyst ($AlCl_3$) in a 1:1.2:1.1 molar ratio, respectively. Derivatives **4a**, **5a, b** and **5f** were purified by distillation in a micro-Claisen distillation apparatus with a fused-on Liebig condenser; compounds **4b, c**, **5c–e** and **5g, h** were recrystallized from hexane. All products were > 98% pure by GC. Physical, GC/MS and ^{1}H NMR data are reported in Table 1, 2 and 3, respectively.

Hydrodehalogenations (Compounds 6a–c and 7a–h); General Procedure:

In a 250-mL three-necked, round-bottomed flask, thermostated at the reaction temperature (50 or 30 ± 0.1 °C) and connected with a system for the addition of H_2, a mixture of aq KOH soln (4.0 mL; 50%), 5% Pd/C (0.512 g; 0.24 mmol of Pd), and Aliquat 336 (0.68 g; 1.6 mmol) was magnetically stirred at about 1000 rpm. A volume of 100 mL of the specific organic solution (2.0 g of the corresponding halogenated substrate dissolved in isooctane) was added. H_2 was bubbled at atmospheric pressure into the organic phase at about 1 mL/min. In the case of compounds **6b, c, 7c–e** and **7g, h**, the reagent amounts were dissolved by ultrasound in isooctane. Reaction times are reported in Table 4. The mixture was filtered and washed with Et_2O and H_2O. The filtrate was extracted with Et_2O (3 × 60 mL) and the combined extracts were dried (Na_2SO_4). After the solvent removal by rotary evaporation, the residue was purified by gravity column chromatography (gradient elution; compounds **6a–c** and **7a–h**; eluent: light petroleum/Et_2O 80:20). Compounds **6a, b, 7a–d** and **7g** were distilled in a micro-Claisen distillation apparatus with a fused-on Liebig condenser. Compounds **6c, 7e, f** and **7h** were recrystallized from hexane. All compounds were > 98% pure by GC. Physical, GC/MS and ^{1}H NMR data are reported in Table 4, 5 and 6, respectively.

NOE Analysis of the Mixture of Isomers 4c and 4′c (4,5-Dichloro-2,2′-dimethyl- and the 5,6-Dichloro-2,2′-dimethylbenzophenones, Entry 6, Table 1).

NOE determinations were recorded as reported in literature.[38]

In the aliphatic region four methyl resonances are detected, recognized by the different intensities. The resonances of the major isomer are at $\delta = 2.36$ and 2.46, those of the minor one at $\delta = 2.17$ and 2.73.

Major isomer: The saturation of the methyl resonance at $\delta = 2.46$ brings about a relevant enhancement of an aromatic doublet at $\delta = 7.30$, but also a minor enhancement of an aromatic singlet at $\delta = 7.36$. On the other hand, the saturation of the methyl at $\delta = 2.36$ causes the strong enhancement of a different singlet at $\delta = 7.38$ and the weaker one of a doublet at $\delta = 7.29$. Only the isomer **4c** (4,5-dichloro-2,2′-dimethylbenzophenone) can accomodate for the presence of two aromatic singlets. The NOEDS analysis also allows the assignment of the methyl resonances 2 and 2′ and of aromatic protons 3, 6, 3′, and 6′. The enhancement of proton 6 at $\delta = 7.36$ upon saturation of the methyl 2′ at $\delta = 2.46$ belonging to the other ring, and the similar enhancement of proton 6′ at $\delta = 7.29$ from saturation of the methyl 2 at $\delta = 2.36$, further suggest that in the preferred conformations the two aromatic rings are not coplanar, in a situation where the methyl groups may come near to the *ortho* protons in the other ring.

Minor isomer: In this isomer the saturation of the methyl resonance at $\delta = 2.17$ induces a strong enhancement of a doublet at $\delta = 7.12$ and a weaker one of a doublet at $\delta = 7.33$, while the saturation of the other methyl at $\delta = 2.73$ gives rise to the sole enhancement of a doublet at $\delta = 7.34$. Only the structure **4c′** (5,6-dichloro-2,2′-dimethylbenzophenone), also in nonplanar conformation, can explain these findings.

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