

Progress in the Palladium-Catalyzed α -Arylation of Ketones with Chloroarenes

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Abstract: Non- and deactivated chloroarenes can be coupled with a wide range of ketones to yield the corresponding arylmethyl ketones in good to excellent yields using a palladium(II) acetate/*n*-BuPd₂ catalyst system. Depending on the ketone, the

chloroarene/ketone ratio and the base, mono or diarylation can be effected selectively.

Keywords: arylation; aryl chlorides; homogeneous catalysis; ketones; palladium.

Introduction

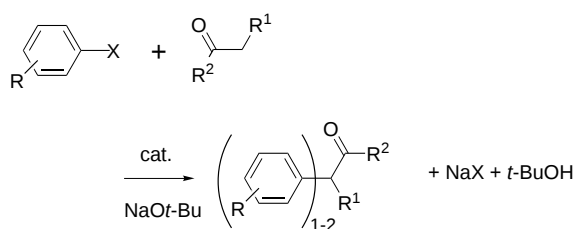
Palladium-catalyzed coupling reactions of aryl halides have gained enormous popularity for the synthesis of organic building blocks, pharmaceutical and agrochemical derivatives, and natural products in the last decade. In addition to the interest in small-scale applications (< 1 g to 100 g), there is an increasing use of this type of reactions for an industrial fine chemical synthesis (1 to > 100 t/a).^[1] In general, there are two important economical prerequisites to apply palladium-catalyzed coupling reactions on a larger scale: a) the starting materials must be easily available and economically attractive, and b) catalyst efficiency is important due to the high price of palladium compounds. Hence, the most interesting raw materials for further refinement are aryl chlorides, and in certain cases bromides and anilines (*via in situ* diazotization). Regarding catalyst efficiency turnover numbers > 1000 and activities > 200 h⁻¹ are more or less a minimum requirement in order to be of interest for practical applications. In order to develop palladium-catalyzed coupling reactions of aryl halides to a practical level together with Herrmann and co-workers we started a program towards more productive palladium catalysts in 1994. As an initial result the so-called palladacycle was introduced as stable and robust palladium catalyst.^[2] While this catalyst gives extremely

high turnover numbers for different coupling reactions of activated and unactivated aryl bromides (after optimization in general TON > 100,000), the reactivity for aryl chlorides, especially neutral and electron-rich ones is not sufficient to allow industrial applications. Hence, we^[3] and other research groups^[4] developed palladium catalysts based on sterically hindered basic phosphines, which are more active and productive. In this respect we were the first who introduced alkyladamantylphosphines as ligands for active palladium catalysts. The high activity of these ligands when applying aryl chlorides as substrates has been demonstrated in Suzuki,^[5] Heck^[6] and palladium-catalyzed amination reactions.^[7] Here, we present for the first time the use of alkyladamantylphosphines in palladium-catalyzed α -arylations of ketones.

The arylation of ketones and other carbonyl compounds at the α -position allows a direct access to various benzylic carbonyl compounds. Recently, versatile palladium-catalyzed α -arylations of ketone enolates^[8] have been developed elegantly by Buchwald,^[9] Hartwig,^[10] and Miura^[11] (Scheme 1).

While Miura et al. reported that PdCl₂ and Cs₂CO₃ allowed the coupling of benzyl ketones with aryl iodides and bromides, Buchwald et al. and Hartwig et al. proposed the use of Pd₂(dba)₃ in the presence of chelating ligands (BINAP and DPPF derivatives) and alkoxide as catalyst systems for the arylation of a variety of ketones. By using chiral (*S*)-BINAP as ligand it is also possible to achieve asymmetric α -arylation using aryl bromides.^[12] Later on it was demonstrated that more reactive arylation systems can be built with sterically hindered di- and monophosphines such as PCy₃, P(*t*-Bu)₃, and DtBPF [1,1-bis(di-*tert*-butylphosphino)ferrocene].^[13]

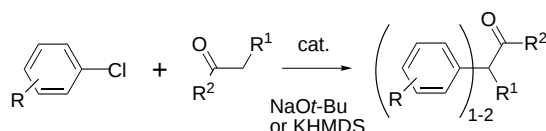
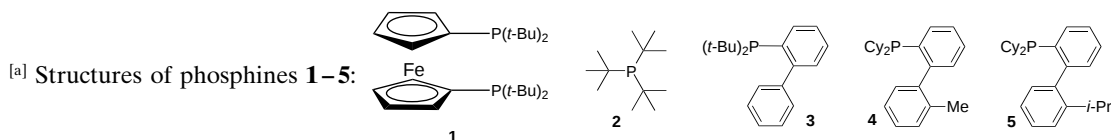
Most protocols for the palladium-catalyzed α -arylation of ketones are based on strong (and more expen-



Scheme 1. α -Arylation of ketones with aryl halides.

Table 1. Overview of chloroarene activation in ketone α -arylation reactions (Scheme 2).

Entry	Author	R	R ¹ /R ² (ketone)	Catalyst ^[a]	Yield [%]	TON
1	Hartwig (1999) ^[13]	H	Me/Ph	Pd(dba) ₂ / 1	86	43
2	Hartwig (1999) ^[13]	H	Me/Ph	Pd(OAc) ₂ / 2	90	45
3	Hartwig (1999) ^[13]	3-OMe	Me/ <i>i</i> -Pr	Pd(dba) ₂ / 1	78	39
4	Hartwig (1999) ^[13]	2-Me	Me/Ph	Pd(dba) ₂ / 1	80	40
5	Hartwig (1999) ^[13]	4-OMe	Me/Ph	Pd(OAc) ₂ / 2	91	46
6	Buchwald (2000) ^[14]	4-Me	Me/Ph	Pd(OAc) ₂ / 3	91	91
7	Buchwald (2000) ^[14]	4-OMe	Me/Me	Pd(OAc) ₂ / 4	74	370
8	Buchwald (2000) ^[14]	4-COMe	Me/Ph	Pd(OAc) ₂ / 5	76	76
9	Buchwald (2000) ^[14]	4-COMe	cyclohexanone	Pd(OAc) ₂ / 4	70	70

**Scheme 2.**

sive) bases NaOt-Bu and KHMDS. However, a small number of arylations with aryl bromides bearing base-sensitive side chains and with the strongly activated, yet base-sensitive *p*-chloroacetophenone were made possible by using K₃PO₄ as base in combination with a catalyst system based on bulky basic phosphines.^[14]

Economically most interesting aryl chlorides have also been used very recently as substrates for ketone arylation in a few cases. As shown in Scheme 2 and Table 1 again the use of bulky phosphines is crucial for the success of these coupling reactions. In most cases acetophenone was used as substrate, however acetone, cyclohexanone and *iso*-propyl methyl ketone also gave good yields of the arylated products. The best catalyst turnover number (TON = 930) was reported for the reaction of α -tetralone with 2-chloro-*p*-xylene.^[14] So far, all reactions of non-activated and deactivated chloroarenes have been described in the presence of NaOt-Bu.

Results and Discussion

In spite of the synthetic utility and the generality of the palladium-catalyzed ketone enolate arylation there is a need for further improvements to make this method applicable on a larger scale, especially if one would like to apply aryl chlorides for this reaction. On the one hand more productive palladium catalysts are desirable for this kind of reaction. On the other hand the use of less costly bases would constitute an important advancement.

Considering the success of PCy₃ and P(*t*-Bu)₃ in previous palladium-catalyzed arylations of ketones it seemed likely to us that alkyladamantylphosphines would be "good" ligands for a number of these reactions, too. However, Buchwald et al. demonstrated clearly that the outcome of the reaction of aryl bromides with different ketones is very much dependent on the substrate combination.^[14] Hence, we commenced the testing of our standard ligand *n*-butylbis(1-adamantyl)-phosphine (*n*-BuPAD₂) in three model reactions using conditions similar to previously reported reactions of aryl bromides.^[13] As model systems the reactions of chlorobenzene and acetophenone, *p*-chlorotoluene and propiophenone, and *p*-chlorotoluene and 3-pentanone were studied. In all reactions toluene was used as solvent and an excess of NaOt-Bu as base. For all model systems variations of the temperature (80–120 °C), the Pd/L ratio, and the catalyst concentration were performed. Selected results are shown in Table 2.

The reaction of chlorobenzene with acetophenone (Table 2, entries 1–5) turned out to be much more sensitive towards variations of reaction parameters compared to the other two test reactions. While total conversion of chlorobenzene is achieved under most conditions used, often unwanted side-products such as benzene and diphenylmethane constitute the major part of products. Optimum results for the synthesis of benzyl phenyl ketone were obtained at a ligand/palladium ratio of 1:1 and a catalyst concentration of 0.1 mol % at 120 °C. Surprisingly, we observed a dramatic influence of the ligand concentration on the reaction outcome. While a yield of 70% of the desired product is obtained at a ligand/palladium ratio of 1:1, the product yield decreased to 32% at a ligand/palladium ratio of 1:2 (Table 2, entries 1 and 2). An even more pronounced effect is detected when an excess of ligand is used. Here, no desired product is observed at a ligand/palladium ratio of 2:1 (Table 2, entry 4). Also at lower catalyst

Table 2. α -Arylation of ketones with Pd(OAc)₂/*n*-BuPAd₂ using NaOt-Bu.^[a]

Entry	Product	Pd conc. [%]	L: Pd	T [°C]	Conv. [%]	Yield [%]	TON
1		0.1	1:2	120	100	32	320
2		0.1	1:1	120	100	70	700
3		0.1	1.5:1	120	100	26	260
4		0.1	2:1	120	100	0	0
5		0.001	2:1	120	10	0	0
6		0.1	1:2	80	98	95	950
7		0.1	1:1	80	100	100	1000
8		0.1	2:1	80	100	100	1000
9		0.1	3:1	80	37	32	320
10		0.05	1:1	80	99	97	1940
11		0.01	1:1	80	41	40	4000
12		0.01	1:1	120	57	41	4100
13		0.1	1:2	80	100	52	520
14		0.1	1:1	80	100	55	550
15		0.1	2:1	80	100	55	550
16		0.1	3:1	80	3	3	30
17		0.01	1:1	80	8	8	80
18		0.01	1:1	120	39	17	1700
19		0.1	1:1	80	100	58	580
20		0.1	1:1	80	66	65	650

^[a] Reaction conditions: 5.0 mmol aryl chloride, 6.0 mmol ketone, 2.2 equiv. NaOt-Bu, 5 mL toluene, 20 h, Pd(dba)₂, *n*-BuPAd₂.

concentrations increased side product formation is observed (Table 2, entry 5).

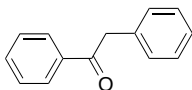
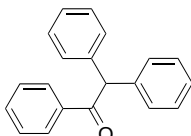
The reaction of propiophenone and *p*-chlorotoluene is less sensitive towards variations of temperature and ligand concentration, although at ligand/palladium ratios >2:1 a significant decrease of the ketone arylation product is observed. Almost quantitative arylation [97% α -(4-methylphenyl)propiophenone] is obtained even at a low catalyst concentration of 0.05 mol %, yielding the highest turnover number (TON = 1940) known for a ketone arylation reaction with non-activated aryl chlorides (Table 2, entry 10). A further decrease of catalyst amount leads to even higher turnover numbers (up to 4000), however, here a drop of product yield occurred.

The arylation of the dialkyl ketone 3-pentanone proceeds in general with lower yields compared to the aromatic ketones (Table 2, entries 13–18). Again an L/Pd ratio of 1:1 and a reaction temperature of 80 °C give

best results. Under these conditions reactions of 3-pentanone with 1,2-dichlorobenzene and α -phenylacetophenone with 4-chlorotoluene proceed in satisfactory yield (58 and 65%, respectively; Table 2, entries 19 and 20).

The results shown in Table 2 demonstrate that the system Pd(dba)₂/*n*-BuPAd₂ allows the coupling of different non-activated aryl chlorides with ketones in good yields at relatively low catalyst concentration. Selectivities for the monoarylated product are good especially if higher substituted alkyl ketones instead of simple methyl ketones are reacted. The strong influence of the ligand concentration demonstrates the importance of low-coordinated palladium(0) complexes for efficient catalysis. In all cases an L/Pd ratio of 1:1 gives the highest product yield, showing that one coordinated ligand is capable of achieving efficient catalysis. In addition, the stability and steric situation of the enolate is important for the outcome of the reaction. Hence,

Table 3. Influence of the base on the activity and selectivity of the reaction of acetophenone with chlorobenzene.^[a]

Entry	Base	Conversion [%]	Yield [%] 	Yield [%] 
1	Na ₂ CO ₃	0	0	0
2	K ₂ CO ₃	75	40	25
3	K ₃ PO ₄	83	16	51
4	Cs ₂ CO ₃	100	22	62
5	CaO	12	0	0

^[a] Reaction conditions: 5.0 mmol aryl chloride, 6.0 mmol ketone, 6.0 mmol base, 5 mL dioxane, 1.0 mol % Pd(OAc)₂, 2.0 mol % *n*-BuPAd₂, 20 h, 100 °C.

propiophenone which gives a more stable enolate compared to acetophenone and 3-pentanone, leads to a higher yield and improved catalyst turnover number. In the case of α -phenylacetophenone the increased steric hindrance must be considered for the lower yield.

Performing a rough economic calculation for the optimized reaction of chlorobenzene with acetophenone it became apparent that, apart from the catalyst (metal and ligand), the base determines the raw material costs of the reaction. Thus, we were interested to find other (especially less costly) bases that allow a general arylation of ketones with aryl chlorides (Table 3). To our delight K₂CO₃, Cs₂CO₃, and K₃PO₄ in dioxane lead to active catalysts at 100 °C giving arylated acetophenones in yields of 65–84%. However, depending on the solubility and pK_b of the base, different ratios of mono- and diarylated products were observed. Here, K₂CO₃ give predominantly the monoarylated product, while Cs₂CO₃ and K₃PO₄ mainly lead to the diarylated product. The formation of significant amounts of diarylated product compared to the reaction with NaOt-Bu as base is explained by the different concentrations of the enolate of the starting material. In general the enolate of the original ketone is less stable compared to the enolate of the arylated product.

Obviously, the selectivity of mono- and diarylated products can be improved by changing the concentration of the starting materials Table 4 (entries 1–3).

In order to prove whether this reactivity is a special feature of the *n*-butylbis(1-adamantyl)phosphine (*n*-BuPAd₂) or if other basic, bulky phosphines show a similar behaviour, we performed further experiments using K₃PO₄ in dioxane at 100 °C with different phosphines [1.0 mol % Pd(OAc)₂, 2.0 mol % ligand].

Table 4 (entries 4–10) shows that not only *n*-BuPAd₂ but a number of sterically hindered basic phosphines (e.g., PCy₃, PhPCy₂) lead to arylated ketones in yields of 60–70%. In all cases mixtures of mono- and diarylated products were obtained. There is no clear trend regard-

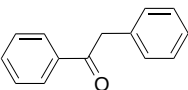
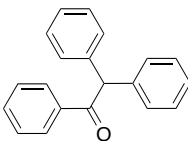
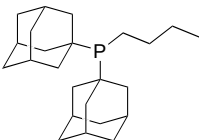
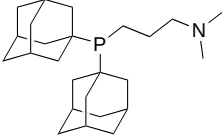
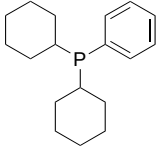
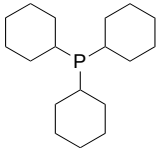
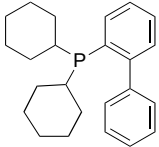
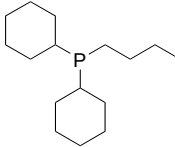
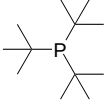
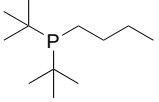
ing steric hindrance and basicity of the phosphine and product yield and selectivity. So far it is unclear why subtle variances in the structure of the ligands cause significant differences in the reaction outcome. Nevertheless, using *n*-BuPAd₂ as ligand the highest yield of α,α -diphenylacetophenone (51%) is obtained on applying standard conditions. By using an excess of chlorobenzene (3 equiv.) this yield can be increased to 62%. On the other hand, a good yield (59%) of the monoarylated product α -phenylacetophenone is obtained using an excess (5 equiv.) of acetophenone (Table 5, entries 1–3).

As shown in Table 5 arylation of acetophenone in the presence of K₃PO₄ is also readily achieved with 4-chloroanisole and 2-chlorofluorobenzene (total yield of arylated products 82 and 80%, respectively). Arylation of α -phenylacetophenone and propiophenone proceeded in high selectivity to yield α -aryl- α -phenylacetophenones and α -arylpropiophenones, respectively, in good to excellent yields (72–99%; Table 5, entries 6–9). Even arylation of 1-indanone with 4-chlorotoluene is possible in the presence of K₃PO₄, yielding the products 2-*p*-tolyl-1-indanone and 2,2-bis(*p*-tolyl)-1-indanone in yields of 42 and 32%, respectively.

In addition, arylations of dialkyl ketones are possible, too. Using a five-fold excess of ketone α -(4-methylphenyl)cyclohexanone and α -(4-methylphenyl)-3-pentanone are obtained in 59 and 60% yield, respectively. Arylation of 3-pentanone with 1,2-dichlorobenzene gave the product 2-(*o*-chlorophenyl)pentan-3-one in 53% yield, demonstrating that one can selectively activate one of two C-Cl bonds.

While arylations of acetophenone and 1-indanone proceeded mainly to doubly arylated products, single arylation is preferentially observed with propiophenone, cyclohexanone and 3-pentanone. In these cases the increased steric hindrance of the monoarylated enolates makes a further arylation reaction difficult.

Table 4. Ligand variation in the reaction of chlorobenzene with acetophenone.^[a]

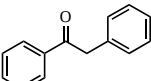
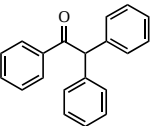
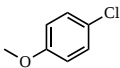
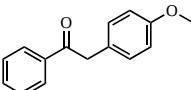
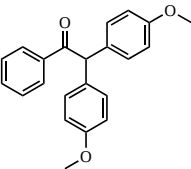
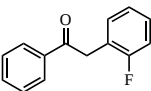
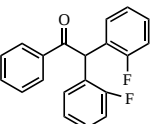
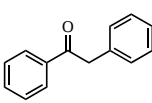
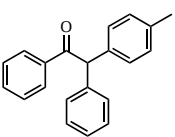
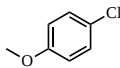
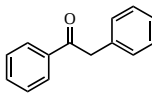
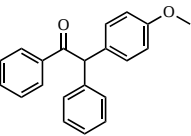
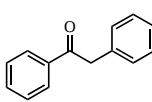
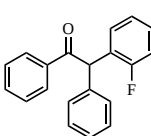
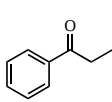
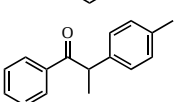
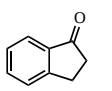
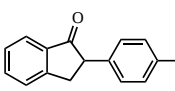
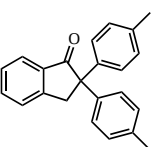
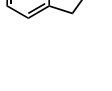
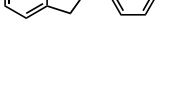
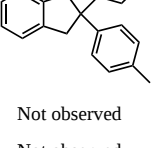
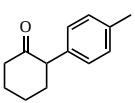
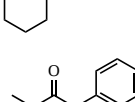
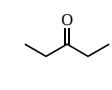
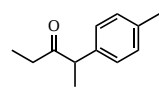
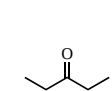
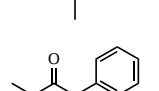
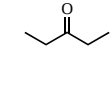
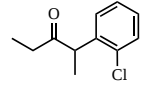
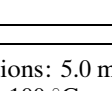
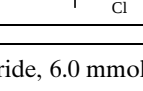
Entry	Ligand	Conversion [%]	Yield [%]	Yield [%]
				
1		83	16	51
2 ^[b]		92	59	31
3 ^[c]		90	22	62
4		68	6	44
5		72	31	31
6		74	33	32
7		50	17	19
8		31	17	3
9		37	0	19
10		44	9	20

^[a] Reaction conditions: 5.0 mmol chlorobenzene, 6.0 mmol acetophenone, 6.0 mmol K_3PO_4 , 5 mL dioxane, 1.0 mol % $Pd(OAc)_2$, 2.0 mol % *n*-BuPAd₂, 100 °C, 20 h.

^[b] 25 mmol acetophenone, 5 mmol chlorobenzene.

^[c] 5 mmol acetophenone, 15 mmol chlorobenzene.

Table 5. α -Arylations of ketones with K_3PO_4 as base.^[a]

Entry	Aryl chloride	Ketone	Conv. [%]	Monoarylated product	Yield [%]	Diarylated Product	Yield [%]
1			83		16		51
2			92 ^[b]		59		31
3			100 ^[c]		22		62
4			100		25		57
5			89		57		23
6			100		99	Not observed	0
7			100		76	Not observed	0
8			100		72	Not observed	0
9 ^[c]			100		90	Not observed	0
10			100		42		32
11			100 ^[c]		26		33
12			100		38	Not observed	0
13			100 ^[b]		59	Not observed	0
14			42		27	Not determined	-
15			71 ^[b]		60	Not determined	-
16			67		37	Not determined	-
17			80 ^[b]		53	Not determined	-

^[a] Reaction conditions: 5.0 mmol aryl chloride, 6.0 mmol ketone, 6.0 mmol K_3PO_4 , dioxane, 1.0 mol % $Pd(OAc)_2$, 2.0 mol % n -BuPAd₂, 20 h, 100 °C.

^[b] Ratio ketone/aryl chloride = 25 mmol/5 mmol.

^[c] Cs_2CO_3 as base.

^[d] 120 °C.

Conclusion

The results presented here demonstrate that Pd/*n*-BuPAd₂ belongs to the most active and productive palladium catalysts for the arylation of ketone enolates using aryl chlorides. Applying NaOt-Bu as base the highest catalyst turnover number known for the arylation with non-activated chloroarenes is reported. In addition, it is shown that less expensive bases such as K₂CO₃ and K₃PO₄ allow ketone arylation, albeit at higher catalyst concentration (1.0 mol %) and lower selectivity. These conditions will be more suitable for substrates with base sensitive functional groups.

Experimental Section

General Procedure

Under an atmosphere of argon 5 mmol of aryl chloride, 6 mmol of ketone, 6 mmol of base, ligand and a palladium source are added to 5 mL of dry toluene or dioxane in a pressure tube. The mixture is heated for 20 h in a bath of silicon oil. After cooling to room temperature the solids are dissolved by addition of 5 mL of methylene chloride and 5 mL of hydrochloric acid (2 M). Diethylene glycol di-*n*-butyl ether or hexadecane are added as an internal standard for gas chromatographic analysis. Products are isolated by distillation or column chromatography (silica gel, hexane/ethyl acetate mixtures).

α -(4-Methylphenyl)propiophenone

¹H NMR (400.1 MHz, CDCl₃, 297 K): δ = 8.33–8.28 (m, 2H), 7.80–7.73 (m, 2H), 7.71–7.66 (m, 2H), 7.64–7.50 (m, 2H), 7.45–7.40 (m, 1H), 5.01 (q, ³J_{H,H} = 6.8 Hz, 1H), 2.61 (s, 3H), 1.88 (d, ³J_{H,H} = 6.7 Hz, 3H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃, 297 K): δ = 200.9, 139.0, 137.0, 137.0, 133.2, 130.2, 129.3, 128.9, 128.1, 47.9, 21.5, 20.0; MS (E.I., 70 eV): m/z = 224 (M⁺), 119, 105; IR (KBr): ν = 1683, 1513, 1448, 1223, 953, 736, 690, 549 cm⁻¹.

α -(4-Methylphenyl)pentan-3-one

¹H NMR (400.1 MHz, CDCl₃, 297 K): δ = 7.03–6.96 (m, 4H), 3.61 (q, ³J_{H,H} = 7.0 Hz, 2H), 2.29–2.22 (m, 1H), 2.20 (s, 3H), 1.26 (d, ³J_{H,H} = 7.0 Hz, 3H), 0.84 (t, ³J_{H,H} = 7.3 Hz, 3H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃, 297 K): δ = 211.9, 138.4, 137.0, 130.0, 128.1, 52.7, 34.5, 21.4, 18.0, 8.4; MS (E.I., 70 eV): m/z = 176 (M⁺), 119; IR (KBr): ν = 2977, 2935, 1716, 1513 cm⁻¹; anal. calcd. for C₁₂H₁₆O: C 81.77, H 9.15%; found: C 81.67, H 9.07%.

α -(2-Chlorophenyl)pentan-3-one

¹H NMR (400.1 MHz, CDCl₃, 297 K): δ = 7.37–7.05 (m, 4H), 4.21 (q, ³J_{H,H} = 7.0 Hz, 2H), 2.30 (q, ³J_{H,H} = 7.3 Hz, 1H), 1.29 (d, ³J_{H,H} = 7.1 Hz, 3H), 0.90 (t, ³J_{H,H} = 7.4 Hz, 3H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃, 297 K): δ = 211.2, 139.1, 134.3, 130.2,

129.0, 128.7, 127.8, 48.9, 35.0, 15.9, 8.4; MS (E.I., 70 eV): m/z = 196 (M⁺), 161, 139, 103, 77, 57; IR (KBr): ν = 3979, 2937, 1718, 1475, 755 cm⁻¹; anal. calcd. for C₁₁H₁₃ClO: C 67.18, H 6.66, Cl 18.03%; found: C 67.27, H, 6.70, Cl 18.56%.

α -Phenyl- α -(4-methylphenyl)acetophenone

¹H NMR (400.1 MHz, CDCl₃, 297 K): δ = 8.05–7.98 (m, 3H), 7.60–7.10 (m, 11H), 6.01 (s, 1H), 2.32 (s, 3H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃, 297 K): δ = 198.8, 139.8, 137.3, 137.3, 136.5, 133.4, 129.9, 129.6, 129.4, 129.4, 129.1, 129.0, 127.5, 59.5, 21.5; MS (E.I., 70 eV): m/z = 286 (M⁺), 233, 196, 105, 77; IR (KBr): ν = 1700, 766 cm⁻¹; anal. calcd. for C₂₁H₁₈O: C 88.08, H 6.34%; found: C 88.11, H, 6.50%.

α,α -Diphenylacetophenone

¹H NMR (400.1 MHz, CDCl₃, 297 K): δ = 7.96–7.88 (m, 2H), 7.46–7.39 (m, 1H), 7.36–7.29 (m, 2H), 7.28–7.13 (m, 10H), 5.96 (s, 1H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃, 297 K): δ = 198.6, 139.5, 137.2, 133.5, 129.6, 129.4, 129.2, 129.0, 127.6, 59.9; MS (E.I., 70 eV): m/z = 272 (M⁺), 167, 105; IR (KBr): ν = 1680, 1595, 1494, 1448, 1206, 765, 750, 740, 695, 683, 613, 564 cm⁻¹; anal. calcd. for C₂₀H₁₆O: C 88.20, H 5.92%; found: C 88.23, H 6.20%.

α,α -Bis(4-methoxyphenyl)acetophenone

¹H NMR (400.1 MHz, CDCl₃, 297 K): δ = 8.12–8.05 (m, 2H), 7.63–7.58 (m, 1H), 7.54–7.48 (m, 2H), 7.30–7.25 (m, 4H), 7.00–6.90 (m, 4H), 6.04 (s, 1H), 3.88 (s, 6H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃, 297 K): δ = 199.2, 159.0, 137.3, 136.1, 133.3, 130.5, 129.4, 129.0, 114.5, 58.2, 55.7; MS (E.I., 70 eV): m/z = 332 (M⁺), 227, 142, 105; IR (KBr): ν = 1692, 1515, 1245, 1179, 1036, 793, 756, 692 cm⁻¹; anal. calcd. for C₂₂H₂₀O₃: C 79.50, H 6.06%; found: C 79.11, H 6.44%.

α -(2-Fluorophenyl)acetophenone

¹H NMR (400.1 MHz, CDCl₃, 297 K): δ = 7.85–7.83 (m, 2H), 7.42–7.36 (m, 1H), 7.34–7.26 (m, 2H), 7.13–7.05 (m, 2H), 7.00–6.88 (m, 2H), 4.17 (s, 1H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃, 297 K): δ = 196.7, 161.5 (d, ¹J_{C,F} = 245.1 Hz), 136.9, 133.8, 132.2 (d, ³J_{C,F} = 4.8 Hz), 129.2, 129.4 (d, ³J_{C,F} = 8.6 Hz), 128.9, 124.7, 122.3 (d, ²J_{C,F} = 15.3 Hz), 115.8 (d, ²J_{C,F} = 21.0 Hz), 39.1; ¹⁹F NMR (235.4 MHz, CDCl₃, 297 K): δ = –116.7; MS (E.I., 70 eV): m/z = 214 (M⁺), 105; IR (KBr): ν = 1687, 1493, 1337, 1237, 1215, 997, 771, 764, 750, 689 cm⁻¹; anal. calcd. for C₁₄H₁₁FO: C 78.49, H 5.18%; found: C 78.31, H 5.33%.

α,α -Bis(2-fluorophenyl)acetophenone

¹H NMR (400.1 MHz, CDCl₃, 297 K): δ = 8.22–8.15 (m, 2H), 7.72–7.66 (m, 1H), 7.64–7.56 (m, 2H), 7.50–7.40 (m, 2H), 7.35–7.20 (m, 6H), 6.77 (s, 1H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃, 297 K): δ = 196.6, 160.4 (d, ¹J_{C,F} = 247.0 Hz), 135.9 (d, ²J_{C,F} = 17.9 Hz), 133.4, 130.6 (d, ⁴J_{C,F} = 3.8 Hz), 129.4 (d, ³J_{C,F} = 8.6 Hz), 128.8 (d, ³J_{C,F} = 9.5 Hz), 124.8, 124.8, 124.4, 124.4,

115.7 (d, $^2J_{\text{C,F}} = 22.0$ Hz), 44.7; ^{19}F NMR (235.4 MHz, CDCl_3 , 297 K): $\delta = -116.2$; MS (E.I., 70 eV): $m/z = 308$ (M^+), 203, 201, 105; IR (KBr): $\nu = 1683, 1489, 1456, 1448, 1235, 1223, 1209, 757, 687$ cm^{-1} ; anal. calcd. for $\text{C}_{20}\text{H}_{14}\text{F}_2\text{O}$: C 77.91, H 4.58%; found: C 77.95, H 4.82%.

α -(4-Methoxyphenyl)- α -phenylacetophenone

^1H NMR (400.1 MHz, CDCl_3 , 297 K): $\delta = 7.94\text{--}7.88$ (m, 2H), 7.45–7.08 (m, 10H), 6.80–6.75 (m, 2H), 5.91 (s, 1H), 3.68 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100.6 MHz, CDCl_3 , 297 K): $\delta = 198.9, 159.1, 139.9, 137.3, 133.4, 131.6, 130.6, 129.5, 129.4, 129.1, 129.0, 127.5, 114.6, 59.0, 55.7$; MS (E.I., 70 eV): $m/z = 302$ (M^+), 197, 153, 105; IR (KBr): $\nu = 1688, 1513, 1446, 1278, 1256, 1207, 1182, 1025, 808, 697, 598$ cm^{-1} ; anal. calcd. for $\text{C}_{21}\text{H}_{18}\text{O}_2$: C 83.42, H 6.00%; found: C 83.36, H 6.28%.

α -(2-Fluorophenyl)- α -phenylacetophenone

^1H NMR (400.1 MHz, CDCl_3 , 297 K): $\delta = 8.35\text{--}8.25$ (m, 2H), 7.82–7.30 (m, 12H), 6.62 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100.6 MHz, CDCl_3 , 297 K): $\delta = 197.7, 160.6$ (d, $^1J_{\text{C,F}} = 246$ Hz), 137.6, 136.8, 133.6, 131.1 (d, $^2J_{\text{C,F}} = 2.9$ Hz), 129.9, 129.4, 129.4, 129.3, 129.1, 127.9, 127.2 (d, $^3J_{\text{C,F}} = 14.3$ Hz), 124.6 (d, $^3J_{\text{C,F}} = 3.8$ Hz), 115.7 (d, $^2J_{\text{C,F}} = 22.0$ Hz), 52.4; ^{19}F NMR (235.4 MHz, CDCl_3 , 297 K): $\delta = -116.5$; MS (E.I., 70 eV): $m/z = 290$ (M^+), 105; IR (KBr): $\nu = 1683, 1486, 1452, 1225, 757, 742, 701$ cm^{-1} ; anal. calcd. for $\text{C}_{20}\text{H}_{15}\text{FO}$: C 82.74, H 5.21%; found: C 82.68, H 5.46%.

2-(4-Methylphenyl)indan-1-one

^1H NMR (400.1 MHz, CDCl_3 , 297 K): $\delta = 8.80\text{--}8.00$ (m, 8H), 4.83 (dd, $^3J_{\text{H,H}} = 4.1$ Hz, $^3J_{\text{H,H}} = 8.2$ Hz, 1H), 4.64 (dd, $^3J_{\text{H,H}} = 8.3$ Hz, $^2J_{\text{H,H}} = 17.2$ Hz, 1H), 4.22 (dd, $^3J_{\text{H,H}} = 3.9$ Hz, $^2J_{\text{H,H}} = 17.2$ Hz, 1H), 3.29 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100.6 MHz, CDCl_3 , 297 K): $\delta = 206.1, 154.1, 137.1, 136.7, 135.4, 130.0, 128.1, 126.9, 126.8, 125.6, 124.9, 53.5, 36.3, 21.5$; MS (E.I., 70 eV): $m/z = 222$ (M^+), 207, 193, 178; IR (KBr): $\nu = 1681, 1448, 1204, 791, 756, 737, 698, 684, 604$ cm^{-1} ; HRMS calcd. for $\text{C}_{16}\text{H}_{14}\text{O}$: 222.10446; found: 222.10539.

2,2-Bis(4-methylphenyl)indan-1-one

^1H NMR (400.1 MHz, CDCl_3 , 297 K): $\delta = 7.75\text{--}6.98$ (m, 12H), 3.81 (s, 2H), 2.22 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100.6 MHz, CDCl_3 , 297 K): $\delta = 206.1, 152.5, 141.0, 136.7, 136.2, 135.6, 129.5, 128.5, 128.3, 126.3, 125.5, 62.6, 45.3, 21.4$; MS (E.I., 70 eV): $m/z = 312$ (M^+), 297, 252, 220, 178, 126, 57; IR (KBr): $\nu = 1707, 1603, 1511, 815, 768$ cm^{-1} .

α -(4-Methylphenyl)cyclohexanone

^1H NMR (400.1 MHz, CDCl_3 , 297 K): $\delta = 7.12\text{--}7.04$ (m, 2H), 7.00–6.92 (m, 2H), 3.53–3.48 (m, 1H), 2.50–1.40 (m, 8H), 2.26 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100.6 MHz, CDCl_3 , 297 K): $\delta = 211.0, 136.9, 136.1, 129.5, 128.8, 57.4, 42.6, 35.5, 28.3, 25.8, 21.5$; MS (E.I., 70 eV): $m/z = 188$ (M^+), 144, 91; IR (KBr): $\nu = 2937, 2859,$

1707, 806 cm^{-1} ; anal. calcd. for $\text{C}_{13}\text{H}_{16}\text{O}$: C 82.94, H 8.57%; found: C 82.84, H 8.27%.

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