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IRON PENTACARBONYL MEDIATED COUPLING OF BENZYL HALIDES TO KETONES UNDER MILD PHASE TRANSFER CONDITIONS.

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SUMMARY

In a two-phase system (saturated aqueous calcium hydroxide, tetrabutylammonium sulfate, dichloromethane, iron pentacarbonyl) benzyl bromides are readily carbonylated to dibenzyl ketones ; α-α' dibromoorthoxylene yields the o-quinodimethane iron tricarbonyl complex 8. It is inferred that the reactions proceed through transient generation of the tetracarbonyl ferrate dianion.

There is now increasing interest in synthetic applications of metal carbonyls under phase transfer conditions[1]. We recently showed that, under such conditions, iron pentacarbonyl is a valuable catalyst for the carbonylation of benzyl halides 1 to arylacetic acids 3[2]. Here we wish to report that under a nitrogen atmosphere, and using a mildly basic aqueous medium, this system conveniently gives the symmetrical ketones 2 (reaction 1).

$$\underset{\underline{1}}{ArCH_2X\ (X = Cl,Br)} \xrightarrow[\text{liquid-liquid phase transfer system}]{Fe(CO)_5\text{, base, cationic carrier}} \underset{\underline{2}}{ArCH_2COCH_2Ar} \quad (1)$$

These results are at variance with a previous report stressing the necessity of a high concentration of sodium hydroxide to obtain ketones 2 in high yields[3]. Furthermore, this method is a valuable alternative to other processes including the slow thermal reaction of 1 with $Fe_2(CO)_9$ or $Fe_3(CO)_{12}$[4], or the use of the highly toxic nickel tetracarbonyl[5].

Several attempts (table I, entries 1, 2, 3) showed us that an atmosphere of carbon monoxide, or the use of a strongly alkaline aqueous medium (NaOH 1M, pH 14) gave poor selectivity and significant production of acid 3. We found (table I, entry 4) that an inert atmosphere and a stable, mildly basic aqueous medium (saturated $Ca(OH)_2$, pH 12.6 at 20°C)

Table I. Synthesis of dibenzyl ketones 2.

Entry	RX 1	Catalytic medium[*] base, N_2 or CO	Reaction time (hours)	Yields[**]				
				RCOR 2	RR 4	RH 5	RCO_2H 3	RCO_2R 6
1	$C_6H_5CH_2Br$	H_2O/CH_2Cl_2 NaOH 1M N_2	0.5	53	6	6	36	
2	id.	$H_2O/C_6H_5CH_3$ $\cdot Ca(OH)_2$ CO (1 Atm)	6	41	2		38	1
3	id.	H_2O/CH_2Cl_2 $Ca(OH)_2$ CO (50 Atm)	1.5	7	5	0	70	6
4	id.	H_2O/CH_2Cl_2 $Ca(OH)_2$ N_2	3	78	0	0	22	0
5	$C_6H_5CH_2Cl$	id.	3.5	30[†]	16		8	7
6	$pCH_3C_6H_4CH_2Br$	id.	1.5	84	0		12	0
7	$pBrC_6H_4CH_2Br$	id.	23	62	5		4	11
8	$pNCC_6H_4CH_2Br$	id.	1.5	0[‡]				
9	β-Napthyl CH_2Br	id.	21	46		22	17	

[*] $Fe(CO)_5/RX$ ratio 1/2, except in run 2 : 1/5 ; 20°C, except in runs 2 and 5 (35°).

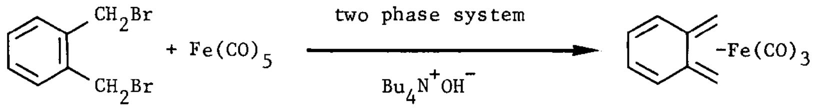
[**] in % of benzyl halide introduced. Determined by ^1H NMR and GC for 2, 4, 5, 6, and by weight for 3. Further characterization by IR and MS.

[†] 15 % 1 unreacted.

[‡] unidentified insoluble polymers.

provided good selectivity to ketones 2. Other runs indicated the lower reactivity of chlorides (entry 5), the unfavourable effect of an electrowithdrawing group (entry 8) and the very favourable effect of an electrodonating group (entry 6). The following standard conditions were typical : into a thermostated cell (20°C) were introduced 4 mmol $Ca(OH)_2$ and 0.5 mmol $Bu_4N^+HSO_4^-$. The cell was purged by several vacuum-nitrogen filling cycles. Desaerated solvents (10 mL water, 10 mL dichloromethane) were then introduced with the benzyl halide (2 mmol) and iron pentacarbonyl (1 mmol). After vigourous stirring (1200 r.p.m.) until complete disappearance of the halide (G.C.), iron carbonyl wastes were destroyed by aerial oxidation, and the crude ketones 2 purified by T.L.C. The acids 3 were extracted from the aqueous and solid phases after acidification.

Looking for the true reactive species in the phase transfer system, we ruled out $Fe(CO)_5$ itself since it did not give any reaction with benzyl bromide under homogeneous conditions (CH_2Cl_2 or $C_6H_5CH_3$ at 20°C for 3 h). Phase transfer generation of the ion pair $Bu_4N^+HFe(CO)_4^-$ is also at variance with observed results, since under homogeneous conditions (CH_2Cl_2, 20°C under CO) this ion pair reacts rapidly with benzyl bromide to give toluene and iron pentacarbonyl. Therefore we suspected that the true reagent was the very basic (about the same as OH^-) tetracarbonyl ferrate dianion $Fe(CO)_4^{--}$, *transiently* generated from iron pentacarbonyl under phase transfer conditions. Therefore, we tried to "trap" it as a stable organometallic derivative. We observed that complex 8 could be generated by reaction of α-α' dibromoorthoxylene 7 with dry preformed $Na_2Fe(CO)_4$[6]. Several attempts under phase transfer conditions (H_2O/CH_2Cl_2 or $H_2O/C_6H_5CH_3$; NaOH or $Ca(OH)_2$, $Bu_4N^+HSO_4^-$ under N_2 from -5° to +50°C) (reaction 2) showed the presence of complex 8 in the organic layer (detected by IR spectroscopy). The following conditions gave the best results (25 % Y. of 8) :



7 8 (2)

$H_2O/C_6H_5CH_3$, NaOH 1.25 M, $Bu_4N^+HSO_4^-$ at +20°C under nitrogen, and slow addition (3 h) of $Fe(CO)_5$ under stirring. The isolated complex 8 gave IR, ^1H NMR and MS data fully consistent with those of the literature[7]. Here also, this complex could not arise from phase transfer production of $Bu_4N^+HFe(CO)_4^-$ since, under homogeneous conditions (CH_2Cl_2 under CO) this ion pair quickly reacted with 7 to give essentially orthoxylene and $Fe(CO)_5$.

Thus, it is reasonable to infer that $Fe(CO)_4^{--}$ is transiently generated from iron pentacarbonyl under mildly basic phase transfer conditions. As a tetrabutylammonium ion pair in the organic phase, it then reacts quickly with the reactive benzyl halide according to the sequence previously demonstrated for other halides in a dry, homogeneous medium with preformed $Na_2Fe(CO)_4$ (reaction 3)[8].

$$\mathrm{ArCH_2Br + Fe(CO)_4^{--} \longrightarrow [ArCH_2Fe(CO)_4]^- \rightleftharpoons [ArCH_2COFe(CO)_3]^- \xrightarrow{ArCH_2Br} ArCH_2COCH_2Ar} \qquad (3)$$

REFERENCES AND NOTES

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   In our hands, an experiment carried out with benzyl bromide strictly according to conditions described in ref. 3 (H_2O/C_6H_6, NaOH 33 %, $Bu_4N^+Br^-$, stirring for 3 h at room temperature under N_2) gave 61 % ketone 2 (instead of 94 % claimed), 6 % toluene and 24 % acid 3 (the latter two products were not reported by these authors).
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