

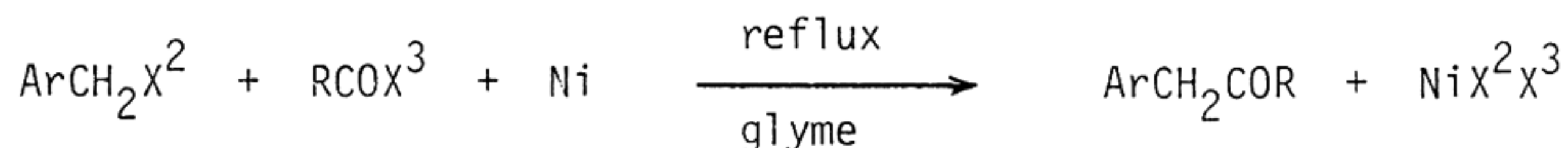
METALLIC NICKEL: A COUPLING REAGENT OF BENZYL HALIDES
AND ACYL HALIDES TO YIELD BENZYL KETONES

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Summary: Metallic nickel was found to be a convenient reductive coupling reagent for the preparation of benzyl ketones by the reaction of benzyl halides with acyl halides.

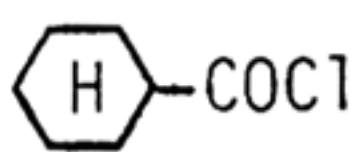
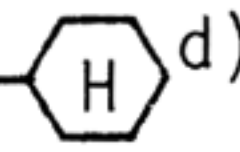
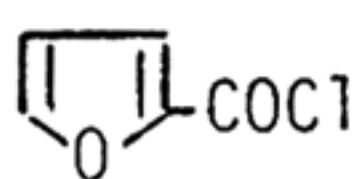
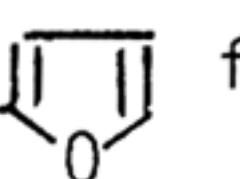
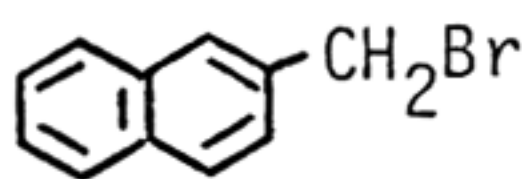
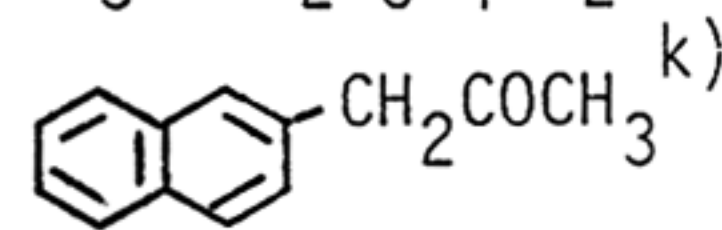
The coupling reaction of acyl halides with organometallic reagents such as organomagnesium, zinc, cadmium,¹⁾ and copper²⁾ compounds is an extremely useful tool for the synthesis of ketones. Recently, palladium-phosphine complexes have been employed as catalysts for the reaction with organozinc,³⁾ tin,⁴⁾ and mercury⁵⁾ compounds utilizing easy oxidative addition of acyl halides to palladium. In a previous communication, we reported that the oxidative addition of benzyl halides to metallic nickel proceeded smoothly to give homo-coupled products.⁶⁾ We now report that the cross-coupling reaction of benzyl halides with acyl halides can be mediated by metallic nickel to afford benzyl ketones.



Metallic nickel was prepared in glyme (25 ml) by the reduction of nickel iodide (2.97 g, 9.50 mmol) with lithium (0.152 g, 21.9 mmol) using naphthalene (0.122 g, 0.95 mmol) as an electron carrier. After stirring these reagents under an atmosphere of argon at room temperature for 12 hr, the finely divided nickel appeared as a black powder which settled in a clear colorless solution. To the nickel powder in refluxing glyme, a mixture of benzyl chloride (0.916 g, 7.24 mmol) and benzoyl chloride (1.07 g, 7.61 mmol) in glyme (10 ml) was added dropwise for 30 min. Additional heating was continued for 15 min and the red-brown reaction mixture was poured into separatory funnel containing 3% hydrochloric acid solution (100 ml) and was extracted with chloroform. The aqueous phase was extracted with chloroform and the combined extracts were washed with water, dried over anhydrous sodium sulfate, and concentrated. Crude oil was submitted on silica gel chromatography eluted with chloroform to give benzyl phenyl ketone (1.04 g, 73%); Mp 55-56°C (lit.⁷⁾ mp 56°C). Bibenzyl formed by the homo-coupling reaction of benzyl chloride⁶⁾ was also isolated in 14% yield.

The reductive coupling reaction of benzyl chloride with benzoyl chloride proceeded even at room temperature, however, improved results were obtained under refluxing glyme (at 85°C). The choice of nickel halide reduced was important and metallic nickel prepared from nickel iodide, bromide, and chloride gave benzyl phenyl ketone in 73, 42, and 11% yields, respectively. Thus, the reaction of benzyl halides with acyl halides using metallic nickel derived from nickel iodide was

Table I. Coupling reaction of benzyl halides with acyl halides mediated by metallic nickel

Benzyl Halide	Acyl Halide	Conditions	Product ^{a)}	Yield(%) ^{b)}
$C_6H_5CH_2Cl$	C_6H_5COCl	r.t., 12 hr	$C_6H_5CH_2COC_6H_5$	54
$C_6H_5CH_2Cl$	C_6H_5COCl	50°C, 3 hr	$C_6H_5CH_2COC_6H_5$	61
$C_6H_5CH_2Cl$	C_6H_5COCl	85°C, 15 min	$C_6H_5CH_2COC_6H_5$	73
$C_6H_5CH_2Cl$	CH_3COCl	85°C, 15 min	$C_6H_5CH_2COCH_3$ ^{c)}	68
$C_6H_5CH_2Cl$		85°C, 15 min	$C_6H_5CH_2CO$ -  ^{d)}	55
$C_6H_5CH_2Cl$	C_6H_5 H $C=C$ H $COCl$	85°C, 15 min	$C_6H_5CH_2CO$ - $C=C$ - C_6H_5 ^{e)}	64
$C_6H_5CH_2Br$		85°C, 15 min	$C_6H_5CH_2CO$ -  ^{f)}	39
$C_6H_5CH_2Br$	$CH_3OCOCH_2CH_2COCl$	85°C, 15 min	$C_6H_5CH_2COCH_2CH_2CO_2CH_3$ ^{g)}	55
p-ClC ₆ H ₄ CH ₂ Cl	C_6H_5COCl	85°C, 15 min	p-ClC ₆ H ₄ CH ₂ COC ₆ H ₅ ^{h)}	82
p-NCC ₆ H ₄ CH ₂ Br	CH_3COCl	85°C, 15 min	p-NCC ₆ H ₄ CH ₂ COCH ₃ ⁱ⁾	85
m-BrCH ₂ C ₆ H ₄ CH ₂ Br	CH_3COCl	85°C, 15 min	m-CH ₃ COCH ₂ C ₆ H ₄ CH ₂ COCH ₃ ^{j)}	62
	CH_3COCl	85°C, 15 min	 ^{k)}	62

a) Stretching frequencies of keto-carbonyl groups were observed in the region of 1655-1720 cm^{-1} and NMR signals of methylene protons adjacent to aromatic rings appeared at δ 3.67-4.27 ppm. b) Yield isolated by silica gel chromatography or recrystallization. c) Bp 95-96°C/11 mmHg (lit. bp 101/14 mmHg) d) Bp 102-103°C/0.6 mmHg (lit. bp 138-139°C/5 mmHg) e) Mp 72-73°C (lit. mp 68-70°C) f) Bp 104°C/0.6 mmHg (lit. bp 161-163°C/10 mmHg) g) Bp 110-111°C/0.45 mmHg (lit. bp 150°C/0.01 mmHg)⁸⁾ h) Mp 135-136°C (lit. mp 136.5°C) i) Mp 79-79.5°C (lit. mp 78-80°C) j) Bp 121°C/0.4 mmHg (lit. bp 146°C/3 mmHg) k) Mp 34-35°C (lit. mp 36-37.2°C)

carried out under refluxing glyme and the results are summarized in Table I.

The reaction may be reasonably explained by the smooth oxidative addition of halides to nickel to afford benzylnickel and acylnickel halides. The metathesis of these complexes could give the acylbenzylnickel complex, which upon reductive elimination would yield the benzyl ketone.

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