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ACTIVATED METALLIC NICKEL IN THE PREPARATION OF SYMMETRICAL 1,3-DIARYLPROPAN-2-ONES FROM BENZYLIC HALIDES AND ALKYL OXALYL CHLORIDES

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Oxidative addition of benzylic halides to nickel in the metallic state followed by insertion of carbon monoxide generated from alkyl oxalyl chlorides proceeded smoothly to give symmetrical 1,3-diarylpropan-2-ones in moderate yields.

Carbonylation with group VIII transition metal complexes has been shown to be a powerful tool in organic synthesis because it is easy to undergo oxidative addition of organic halides to transition metals and insertion of carbon monoxide to organotransition metals formed.[1)] Metal carbonyls such as diiron nonacarbonyl,[2-4)] triiron dodecacarbonyl,[4,5)] nickel carbonyl,[6,7)] and dicobalt octacarbonyl[8)] have been employed for the preparation of symmetrical ketones from aryl, benzyl, and arylmercuric halides[9)] in a stoichiometric fashion.[10)] Disodium tetracarbonylferrate[4,11)] or potassium hexacyanodinickelate-carbon monoxide[12)] have also been used for dibenzyl ketone synthesis.

In spite of usefulness of these complexes, it is generally not possible to cause the satisfactory reaction with transition metals in the metallic state[13)] under mild conditions due to their poor reactivity. In a previous communication we reported that activated metallic nickel, prepared by the reduction of nickel halide with lithium, underwent oxidative addition of benzylic halides to give homo-coupled products.[14)] We now report that carbonylation of the oxidative adducts of benzylic halides to the nickel proceeded smoothly to afford symmetrical 1,3-diarylpropan-2-ones in moderate yields, in which the carbonyl groups of alkyl oxalyl chlorides served as a source of carbon monoxide.

$$2\ \mathrm{ArCH_2X} + \mathrm{ClCOCO_2R} \xrightarrow[\text{glyme, 85 }^{\circ}\text{C}]{\text{Metallic Ni}} \mathrm{ArCH_2COCH_2Ar} + 1/2\ \mathrm{RO_2CCO_2R}$$

X = Cl, Br

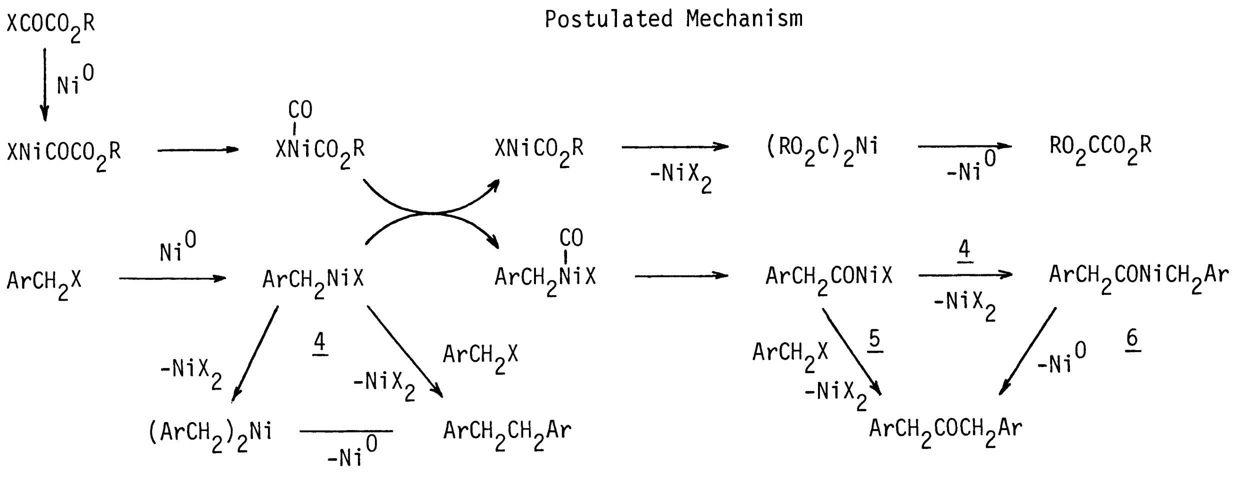
Metallic nickel was prepared in glyme (25 ml) by the reduction of nickel iodide (3.13 g, 10 mmol) with lithium (0.160 g, 23 mmol) using naphthalene (0.128 g, 1 mmol) as an electron carrier.

Table 1. Preparation of Symmetrical 1,3-Diarylpropan-2-ones by the Reaction of Benzylic Halides with Alkyl Oxalyl Chlorides in the Presence of Metallic Nickel a)

Benzyl halide (1)	Alkyl oxalyl chloride (2)	Ratio of 1/2	Product (3) b)	Yield c) %
$C_6H_5CH_2Cl$	$ClCOCO_2C_2H_5$	2.5/1	$C_6H_5CH_2COCH_2C_6H_5$	35 d)
$C_6H_5CH_2Cl$	$ClCOCO_2C_2H_5$	1/1	$C_6H_6CH_2COCH_2C_6H_5$	48
$C_6H_5CH_2Cl$	$ClCOCO_2C_2H_5$	1/2.5	$C_6H_5CH_2COCH_2C_6H_5$	47
$C_6H_5CH_2Cl$	$ClCOCO_2CH_3$	1/1	$C_6H_5CH_2COCH_2C_6H_5$	46
$4\text{-}CH_3C_6H_4CH_2Cl$	$ClCOCO_2C_2H_5$	1/1	$4\text{-}CH_3C_6H_4CH_2COCH_2C_6H_4CH_3\text{-}4$ e)	46
$3\text{-}CH_3OC_6H_4CH_2Cl$	$ClCOCO_2C_2H_5$	1/1	$3\text{-}CH_3OC_6H_4CH_2COCH_2C_6H_4OCH_3\text{-}3$ f)	43
$4\text{-}ClC_6H_4CH_2Cl$	$ClCOCO_2C_2H_5$	1/1	$4\text{-}ClC_6H_4CH_2COCH_2C_6H_4Cl\text{-}4$ g)	54
$4\text{-}BrC_6H_4CH_2Br$	$ClCOCO_2C_2H_5$	1/1	$4\text{-}BrC_6H_4CH_2COCH_2C_6H_4Br\text{-}4$ h)	46
$4\text{-}NCC_6H_4CH_2Br$	$ClCOCO_2C_2H_5$	1/1	$4\text{-}NCC_6H_4CH_2COCH_2C_6H_4CN\text{-}4$ i)	46
$4\text{-}CH_3O_2CC_6H_4CH_2Cl$	$ClCOCO_2C_2H_5$	1/1	$4\text{-}CH_3O_2CC_6H_4CH_2COCH_2C_6H_4CO_2CH_3\text{-}4$ j)	45
$3\text{-}F_3CC_6H_4CH_2Cl$	$ClCOCO_2C_2H_5$	1/1	$3\text{-}F_3CC_6H_4CH_2COCH_2C_6H_4CF_3\text{-}3$ k)	49
$1\text{-}C_{10}H_7CH_2Cl$ l)	$ClCOCO_2C_2H_5$	1/1	$1\text{-}C_{10}H_7CH_2COCH_2C_{10}H_7\text{-}1$ m)	59

a) Reaction was carried out in glyme at 85 °C. b) Carbonyl stretching frequencies were observed in the region of 1700-1710 cm^{-1} and NMR signals of methylene protons appeared at δ3.64-4.07 ppm. c) Isolated yield based on benzylic halide used unless otherwise noted. d) Isolated yield based on ethyl oxalyl chloride used. e) Mp 54-55 °C (lit. 54-55 °C). f) Mp 135.5-136.5 °C (semicarbazone) [(lit. mp 136-136.5 °C (semicarbazone)]. g) Mp 96-97 °C (lit. mp 95-96 °C). h) Mp 119-119.5 °C (lit. mp 116-118 °C). i) Mp 149-150 °C, m/e = 260 (M^+) (lit.17) mp 79 °C). j) Mp 140-141 °C, m/e = 326.1136 Calcd for $C_{19}H_{18}O_5$ 326.1153. k) Mp 53-54 °C, Bp 127 °C/0.47 Torr, m/e = 346.0769 Calcd for $C_{17}H_{12}F_6O$ 346.0792. l) 1-(Chloromethyl)naphthalene. m) Mp 107-107.5 °C (lit. mp 108-109 °C).

After stirring these reagents under an atmosphere of argon at room temperature for 12 h , the finely divided metal appeared as black powders which settled in a clear colorless solution. To the nickel in refluxing glyme (85 °C), a mixture of benzyl chloride (1.01 g, 8.0 mmol) and ethyl oxalyl chloride (1.09 g, 8.0 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 a 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. 1,3-Diphenylpropan-2-one (0.403 g, 48%) was isolated by silica gel chromatography upon elution with chloroform: Bp 125-127 °C/0.8 Torr (lit.5) bp 105-110 °C/0.4 Torr).



Postulated Mechanism

Scheme 1.

The other products were diethyl oxalate (39%) and 1,2-diphenylethane (18%) which was formed by homocoupling reaction of benzyl chloride by metallic nickel.14)

The reaction of benzyl chloride with ethyl oxalyl chloride proceeded at room temperature or at 60 °C, and the yields of 1,3-diphenylpropan-2-one were 11% and 45%, respectively. Thus, the carbonylation was carried out at 85 °C and the results are summarized in Table 1. The stoichiometric ratio of benzylic halide/alkyl oxalyl chloride was 2/1, and most satisfactory results were obtained with a ratio of 1/1.

One possible mechanistic sequence for the present reaction is shown in Scheme 1. The carbon monoxide insertion into the carbon-metal σ bond of alkyltransition metal complexes is well known.15) Thus, the oxidative addition of benzyl halide to metallic nickel gives benzylnickel(II) halide (4) and the insertion of carbon monoxide, which is formed by decarbonylation of alkyl oxalyl chloride, into the benzyl-nickel bond of complex 4, would afford arylacetyl(II) complex (5). The metathesis of complexes 4 and 5 seems to give (arylacetyl)benzylnickel(II) complex (6), which undergoes reductive elimination to yield 1,3-diarylpropan-2-one (3). The formation of 1,2-diarylethane may be expained by the reductive elimination of bisbenzylnickel complex (7) formed by metathesis of benzylnickel complex (4).16) It is also possible that the reaction of benzyl halide with complex 4 or 5 gives homocoupled product or ketone, respectively.

In the dibenzyl ketone synthesis using benzyl halides and transition metal complexes,2-6,11,12) readily available benzyl chlorides were not as reactive, and generally gave poor results (up to 51% yield6)) in spite of effectiveness of benzyl bromides and iodides, and the compatibility with functional groups was not examined. In conclusion these results show that yields are comparable or greater than those using complexes of iron and nickel, and that functional groups such as chloro, bromo, cyano, and carbomethoxy groups are compatible with the reaction conditions employed.

Furthermore, potential utility would be expected in the use of nickel in the metallic state as a reagent in organic synthesis. The generality of this reaction is under investigation and will be reported in the near future.

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