the mixture was freed of ether *in vacuo* yielding the isoxazolium salt as a colorless viscous oil.

A sample of crude IVc prepared on the above scale was dissolved in 20 ml of 10% aqueous $NaHCO_3$. After the vigorous evolution of carbon dioxide had subsided, the mixture was extracted with two 20-ml portions of ether, the combined ether extracts were dried over $MgSO_4$, and the solvent was evaporated cautiously to give a yellow oil which solidified on scratching under a small amount of ether, yield of amide X, 240 mg, 22%. Two recrystallizations from benzene–cyclohexane gave colorless clumps of needles: mp 89–91°; infrared ($CHCl_3$), 2.95, 5.73, and 5.95 μ; nmr, $\delta_{TMS}^{CDCl_3}$ 7.1–7.7 (1 H, envelope), 4.36 (1 H, singlet), 4.27 (4 H, quartet, J = 7 cps), 2.86 (3 H, doublet, J = 5 cps), 1.29 (6 H, triplet, J = 7 cps).

Anal. Calcd for $C_9H_{15}NO_5$: C, 49.76; H, 6.96; N, 6.45; mol wt, 217. Found: C, 50.01; H, 7.03; N, 6.47; mol wt, 217 (mass spectrum).

3-Carboethoxy-4-methylimino-3,4,5,6,7,8-hexahydrocoumarin (VIIb).—Crude 2-methyl-4-carboethoxy-5-ethoxyisoxazolium fluoroborate (IVc), prepared from (VIIIb, 2.55 g, 0.015 mole) as described above, was dissolved in 30 ml of acetonitrile and the solution was cooled in a Dry Ice–acetone bath. Triethylamine (2.25 ml, 0.015 mole) was added dropwise and then 1-pyrrolidinocyclohexene (I,[13] 2.25 g, 0.015 mole) was added in one portion. The mixture was allowed to stand for 16 hr at room temperature under nitrogen. The solvent was removed on a rotary evaporator, the residual gum was dissolved in a mixture of 30 ml of water and 1.8 ml of acetic acid, and the solution was warmed for 5 min on the steam bath. After cooling the mixture was extracted with two 30-ml portions of ether. The extracts were washed with 10% aqueous $NaHCO_3$ and dried over $MgSO_4$ and the solvent was evaporated, yielding an oil which partially crystallized on standing in an evaporating dish. The crystals were triturated with a small amount of ether, filtered, and washed with ether. The light tan prismatic needles (74 mg, 2.0%) were further purified by column chromatography on neutral grade 1 alumina using benzene as eluent. Recrystallization from cyclohexane afforded analytically pure material: mp 106–108°; infrared ($CHCl_3$), 2.90, 6.10, and 6.25 μ; nmr, $\delta_{TMS}^{CDCl_3}$ 4.45 (2 H, quartet, J = 7 cps), 3.44 (3 H, singlet), 2.3–2.8 (4 H, envelope), 1.6–2.1 (4 H, envelope), 1.45 (3 H, triplet, J = 7 cps) (the enolic proton was not detectable).

Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.13; H, 6.82; N, 5.58; mol wt, 251. Found: C, 62.11; H, 6.61; N, 5.39; mol wt, 251 (mass spectrum).

Reaction of 2-Ethylbenzisoxazolium Fluoroborate with 1-Pyrrolidinocyclohexene.—A solution of 2-ethylbenzisoxazolium fluoroborate[10] (XI, 5.4 g, 0.02 mole) in 20 ml of acetonitrile was added dropwise with stirring at room temperature over 30 min to a solution of 1-pyrrolidinocyclohexene (I,[13] 6.0 g, 0.04 mole) in 40 ml of benzene. The mixture was allowed to stand overnight at room temperature under nitrogen and the solvent was then evaporated; the gummy residue was dissolved in 20 ml of 6 *N* HCl and the solution was warmed for 5 min on the steam bath. The mixture turned dark and an oil separated. After cooling, the mixture was extracted with three 20-ml portions of ether, the combined extracts were washed with water and then with 10% aqueous $NaHCO_3$ and dried ($MgSO_4$), and the solvent was evaporated. The resulting oil solidified partially on standing. Chromatographic filtration through a short column of neutral grade I alumina in chloroform and two recrystallizations from cyclohexane gave almost colorless needles of XII (0.5 g, 18%): mp 133–134°; infrared, ($CHCl_3$) 2.91, 3.07, 5.91, and 6.02 μ; nmr, $\delta_{TMS}^{CDCl_3}$ 6.8–8.2 (8 H, multiplet), 6.2–6.7 (1 H, envelope), 3.33 (2 H, quintet, poorly resolved), 1.0 (3 H, triplet, J = 6.5 cps).

Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91; mol wt, 285. Found: C, 67.34; H, 5.07; N, 5.24; mol wt, 285 (mass spectrum).

Registry No.—IIIa, 15129-05-2; VIIa, 15129-06-3; VIIa fluoroborate salt, 12167-68-9; VIIb, 15129-07-4; X, 15129-21-2; XII, 15129-08-5.

Acknowledgment.—This research was supported by a grant from the U. S. Public Health Service (GM 13980).

Reactions of Benzyl Halides with Nickel Carbonyl in Various Media

E. YOSHISATO AND S. TSUTSUMI

Department of Chemical Technology, Faculty of Engineering, Osaka University, Miyakojima-ku, Osaka, Japan

Received August 8, 1967

Recently a number of reports have been published on the reactions of nickel carbonyl with some active halides, such as allylic halides,[1] propargyl halides,[2] or aryl iodides.[3] The types of the reaction products, however, differ with the change in the properties of the ogranic group in the halides. For example, allyl halides form linear dimers on reaction with nickel carbonyl in alcohols or in aprotic solvents. The reactions are considered to proceed *via* π-allylnickel complexes. These π-allylnickel complexes have been shown to react with other organic halides to yield coupling products[4] and also to react with acetylene and carbon monoxide,[5] acrylonitrile,[6] benzaldehyde, acrolein, cyclopentanone, or styrene oxide.[4] Although carbonylation of allyl halides can only be accomplished under high pressure of carbon monoxide, as reported by Bauld, iodobenzene is carbonylated with nickel carbonyl to give esters of benzoic acid in alcoholic solvents and benzil and α,α'-dibenzoyloxystilbene in aprotic solvents. These carbonylation products were considered to be produced by the alcoholysis or thermal decomposition of the postulated intermediate, benzoylnickel carbonylate, $C_6H_5Ni(CO)_nI$, which contains a benzoyl–nickel σ bond. Since the ordinary alkyl halides were reported not to react with nickel carbonyl,[3] it is interesting to select benzyl halide series for reactions with nickel carbonyl. We have carried out the reactions of nickel carbonyl with benzyl halides in various solvents and obtained new types of results (Table I).

As indicated in Table I, carbon monoxide insertion occurred in the polar nonaromatic solvents, whereas almost no insertion occurred in the aromatic solvents. The reactivity of benzyl halides in the carbonylation increased in the order chloride < bromide < iodide and the increasing polarity of the solvent results in the increasing reactivity. Benzyl bromide and iodide were converted mainly into ethyl phenylacetate in ethanol and, when the reaction between benzyl iodide and nickel carbonyl was carried out in tetrahydrofuran, the fission of the tetrahydrofuran ring occurred to give 4-iodo-*n*-butyl ester of phenylacetic acid in a 62% yield. In polar aprotic solvents, such as N,N-dimethylformamide, dimethyl sulfoxide, or acetonitrile, dibenzyl ketone was obtained in an excellent yield, but neither α-diketone nor its derivative (enediol diester) was obtained. It is noteworthy that, when the

---

(1) (a) G. P. Chiusoli, *Angew. Chem.*, **72**, 74 (1960); I. D. Webb and T. Borcherdt, *J. Am. Chem. Soc.*, **74**, 2654 (1951); (b) E. J. Corey and M. F. Semmelhack, *Tetrahedron Letters*, 6237 (1966); E. C. Corey and M. F. Semmelhack, *J. Am. Chem. Soc.*, **89**, 2757 (1967); (c) E. W. Gowling and S. F. A. Kettle, *Inorg. Chem.*, **3**, 605 (1964).

(2) R. W. Rosenthal and L. H. Schwartzman, *J. Org. Chem.*, **24**, 836 (1959).

(3) N. L. Bauld, *Tetrahedron Letters*, 1841 (1963).

(4) E. J. Corey and M. F. Semmelhack, *J. Am. Chem. Soc.*, **89**, 2755 (1967).

(5) G. P. Chiusoli and L. Cassar, *Angew Chem. Intern. Ed. Engl.*, **6**, 124 (1967).

(6) M. Dubini and F. Montino, *J. Organometal. Chem.*, **6**, 188 (1966).

SCHEME I

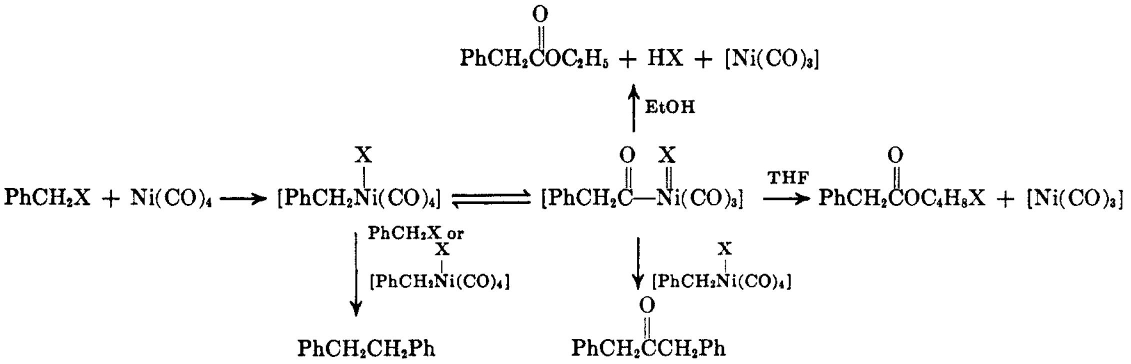

TABLE I

REACTION PRODUCTS FROM BENZYL HALIDES AND NICKEL CARBONYL IN VARIOUS SOLVENTS[a]

Solvent	Halide	Yield of product[b] (%)
EtOH	$\mathrm{PhCH_2Cl}$	No reaction
	$\mathrm{PhCH_2Br}$	Bibenzyl (9), dibenzyl ketone (2), ethyl phenylacetate (71)
	$\mathrm{PhCH_2I}$	Bibenzyl (4), dibenzyl ketone (32), ethyl phenylacetate (57)
Cyclohexane	$\mathrm{PhCH_2Cl}$	No reaction
	$\mathrm{PhCH_2Br}$	No reaction
	$\mathrm{PhCH_2I}$	Bibenzyl (31), dibenzyl ketone (4)
THF[c]	$\mathrm{PhCH_2Cl}$	No reaction
	$\mathrm{PhCH_2Br}$	Bibenzyl (18), dibenzyl ketone (18), 4-bromo-*n*-butyl phenylacetate (2)
	$\mathrm{PhCH_2I}$	Dibenzyl (4), dibenzyl ketone (15), 4-iodo-*n*-butyl phenylacetate (62)
DMF[d]	$\mathrm{PhCH_2Cl}$	Bibenzyl (6), dibenzyl ketone (51)
	$\mathrm{PhCH_2Br}$	Bibenzyl (4), dibenzyl ketone (93)
	$\mathrm{PhCH_2I}$	Dibenzyl ketone (95)
Benzene	$\mathrm{PhCH_2Cl}$	Diphenylmethane (36), dibenzylbenzene (11)
	$\mathrm{PhCH_2Br}$	Diphenylmethane (37), dibenzylbenzene (11)
	$\mathrm{PhCH_2I}$	Diphenylmethane (11), bibenzyl (33), dibenzyl ketone (3)

[a] Reactions of benzyl halide (0.05 mole) and nickel carbonyl (0.05 mole) were carried out in 50 ml of solvent at 50–60° for 50 hr. [b] Based on benzyl halide. [c] Tetrahydrofuran. [d] N,N-Dimethylformamide.

reaction was carried out in nitromethane, which has high dielectric constant as acetonitrile (ϵ 36 at 30°) but has poorer coordinating ability, almost all of the benzyl halide was recovered unreacted. This suggests that the coordinating ability of the solvent is important in the reactions.

From the analogy of previously observed reactions, these carbonylation products can be viewed as arising from the further reaction of the postulated intermediate, phenylacetylnickel complex (Scheme I).

There is another possible way for the formation of ester in ethanol or in tetrahydrofuran: phenylacetyl halide is formed from the phenylacetylnickel complex and followed by the attack of ethanol or tetrahydrofuran to give the ester. Dibenzyl ketone can be formed in two possible ways (and the same situation arises for the formation of bibenzyl): by the reaction between the intermediate phenylacetylnickel complex and benzyl halide or by the reaction between the benzylnickel complex and the phenylacetylnickel complex. When 2 moles of benzyl bromide or iodide were used per mole of nickel carbonyl in N,N-dimethylformamide, just 1 mole of the benzyl halide reacted to give dinenzyl ketone almost exclusively and the remaining 1 mole of benzyl halide was recovered unreacted. The ratio of nickel to bromine of the water extract of the reaction mixture showed 0.97 corresponding to the composition [NiX]. These results favor the latter mechanism since, if the ketone was formed by the former mechanism, 2 moles of benzyl halide should be consumed. This mechanism is similar to that of dialkyl ketone formation by the thermal decomposition of alkylcobalt tetracarbonyls.[7]

In benzene, however, quite a different type of reaction took place. The formation of nickel halide and the evolution of hydrogen halide and carbon monoxide were observed in the course of the reaction and diphenylmethane and higher benzylated compounds were produced. Compared with the carbonylation mentioned above, the order of reactivity of benzyl halide was reversed in an order chloride ~ bromide > iodide. When toluene was used in place of benzene, a higher yield (58%) of benzylation products of toluene was obtained (only *ortho* and *para*, and the ratio of *ortho* to *para* is *ca.* 3:4), but in chlorobenzene the yield was much lower (4%). Thus it appears that these products were formed by a Friedel–Crafts-type reaction; *i.e.*, the halogen is abstracted from benzyl halide by a nickel atom to form the benzyl cation which attacks the aromatic ring, but the actual catalyst is not clear. Anhydrous nickel halide, for which a slight Friedel–Crafts catalytic activity has been claimed,[8] did not react with benzyl bromide under the same reaction conditions.

Benzylation of aromatics was also observed in the reactions of iron pentacarbonyl with benzyl halides in benzene. In another solvent no carbon monoxide inserted compounds were produced; *e.g.*, benzyl bromide and iron pentacarbonyl gave ethyl benzyl ether in ethanol or bibenzyl in N,N-dimethylformamide almost quantitatively, but did not react in tetrahydrofuran or in other solvents.

Experimental Section[9]

Commercially available benzyl chloride and bromide were purified by fractional distillation. Benzyl iodide was prepared

---

[7] R. F. Heck, *Advan. Organometal. Chem.*, **4**, 257 (1966).

[8] B. N. Dolgov, Yu. I. Khudobin, and N. P. Kharitonov, *Bull. Acad. Sci. USSR, Div. Chem. Soc.*, 1238 (1959).

[9] Nmr spectra were taken with a Model JNM-G-60 spectrometer (Japan Electron Optics Laboratory Co.). Infrared spectra were obtained with a Shimazu IR-27C spectrometer. Gas–liquid partition chromatographic analysis were made either with a Yanagimoto GCG 5DH gas chromatograph using a 1.5-m column of SE 30 and 3.75-m column of 5% PEG 20M or with a Hitachi–Perkin-Elmer F6-D gas chromatograph using Z 45 column. Molecular weights were determined in benzene by using a Mechrolab vapor pressure osmometer. Melting points and boiling points are uncorrected.

from benzyl chloride and sodium iodide[10] and purified by recrystallization from ethanol. Nickel carbonyl was prepared by the procedure of Chiusoli and Mondelli.[11] Anhydrous nickel bromide was prepared as described in the literature.[12] Ethanol was dried by magnesium and iodine and then distilled. Tetrahydrofuran was refluxed with sodium and benzophenone until the solution turned blue and was then distilled. Cyclohexane, benzene, and toluene were dried over sodium wire and then distilled. N,N-Dimethylformamide and dimethyl sulfoxide, reagent grade materials, were fractionated and dried over a molecular sieve. Acetonitrile and nitromethane were distilled over phosphorus pentoxide. All solvents were saturated with argon before use. The analysis of nickel and bromide in aqueous solution was performed as described in the text.[13]

General Procedure.—A mixture of 7.5 g (0.05 mole) of nickel carbonyl and 0.05 mole of benzyl halide in 50 ml of solvent was stirred at 50–60° for 50 hr under an atmosphere of argon. The solvent was then removed by an aspirator and the residue was extracted with ether (or the reaction mixture was partitioned between ether and water when N,N-dimethylformamide or dimethyl sulfoxide was used as solvent). The extract was washed with water and dried over anhydrous magnesium sulfate. After the ether was removed the residue was distilled at reduced pressure. The distillate was analyzed and identified by gas–liquid partition chromatography and infrared and nmr spectra with authentic samples. Yields were calculated by gas–liquid partition chromatography and nmr spectra from the relative areas of singlet methylene peaks of benzyl groups.

4-Iodo-*n*-butyl Phenylacetate.—A mixture of 7.5 g (0.05 mole) of nickel carbonyl and 10.9 g (0.05 mole) of benzyl iodide in 50 ml of tetrahydrofuran was treated as described above. Distillation at reduced pressure gave two fractions: fraction 1, 0.9 g, bp 120–140° (0.5 mm); and fraction 2, 10.3 g, bp 145–160° (0.5 mm). Each fraction was analyzed by gas–liquid partition chromatography and infrared and nmr spectra. Fraction 1 was shown to be a mixture of 0.2 g of bibenzyl and 0.6 g of dibenzyl ketone. Fraction 2 was shown to consist of 0.2 g of dibenzyl ketone and 9.8 g of 4-iodo-*n*-butyl phenylacetate. The analytical sample of the ester was obtained by repeated distillation, bp 157–158° (0.5 mm).

Anal. Calcd for $C_{12}H_{15}O_2I$: C, 45.31; H, 4.74; I, 39.89; mol wt, 318. Found: C, 45.45; H, 4.76; I, 40.12; mol wt, 316.

Its nmr spectrum in CCl_4 exhibited a singlet (five protons) at τ 2.82, a triplet (two protons) at 5.99 (J = 6 cps), a singlet (two protons) at 6.51, a triplet (two protons) at 7.06 (J = 6 cps), and a multiplet (four protons) at τ 8.29, consistent with the structure $C_6H_5CH_2COOCH_2CH_2CH_2CH_2I$.

Benzylation of Benzene.—A solution of 7.5 g (0.05 mole) of nickel carbonyl and 6.4 g (0.05 mole) of benzyl chloride in 50 ml of benzene was stirred at 50–60° for 50 hr under argon. The reaction mixture was filtered to remove nickel chloride deposited during the reaction. The filtrate was washed with water and dried over anhydrous magnesium sulfate. Removal of benzene and distillation under vacuum gave the following fractions: fraction 1, 3.3 g, bp 74–75° (0.5 mm); fraction 2, 0.7 g, bp 150–160° (0.5 mm); and 1.3 g of polymeric residue. On standing fraction 1 crystallized. Recrystallization from ethanol provided white needles, mp 26–27°, and no depression resulted on admixture with diphenylmethane (mp 27°). Fraction 2 was shown to be a mixture of dibenzylbenzenes, but the relative amounts of the three isomers were not determined. Three crystallization from ethanol gave white needles: mp 78–80° (melting points of 1,2-, 1,3-, and 1,4-dibenzylbenzene are 78, 59, and 86°, respectively[14]).

Anal. Calcd for $C_{20}H_{18}$: C, 93.02; H, 6.98; mol wt, 258. Found: C, 93.08; H, 7.00; mol wt, 261.

Its nmr spectrum in CCl_4 exhibited a singlet (ten protons) at τ 3.01, a singlet (four protons) at 3.12, and a singlet (four protons) at 6.18.

Benzylation of Toluene.—A mixture of 7.5 g (0.05 mole) of nickel carbonyl and 8.6 g (0.05 mole) of benzyl bromide in 50 ml of toluene was treated in the similar manner described for the benzylation of benzene. The 5.3-g fraction, bp 85–90° (0.7 mm), was shown to be monobenzylation products of toluene by gas–liquid partition chromatography with authentic samples. The authentic samples of *o*-, *m*-, and *p*-benzyltoluene were prepared by coupling reactions between the Grignard reagent of *o*-, *m*-, or *p*-bromotoluene and benzyl chloride. Analysis of the monobenzylation products by gas–liquid partition chromatography using a Z 45 capillary column at 190° showed that only *ortho* (46.6 min) and *para* (48.9 min) isomers were obtained and the relative peak area of *ortho* to *para* was 74:100, which was consistent with the observation from the infrared spectrum.

Registry No.—Nickel carbonyl, 13463-39-3; bibenzyl, 103-29-7; dibenzyl ketone, 102-04-5; 4-iodo-*n*-butyl phenylacetate, 15135-08-7; 1,2-dibenzylbenzene, 792-68-7; 1,3-dibenzylbenzene, 15180-20-8; 1,4-dibenzylbenzene, 793-23-7.

---

[10] F. C. Whitmore and E. N. Thurman, *J. Am. Chem. Soc.*, **51**, 1497 (1929).

[11] G. P. Chiusoli and G. Mondelli, *Chem. Ind.* (Milan), **43**, 259 (1961).

[12] R. B. King, *Organometal. Syn.*, **1**, 71 (1965).

[13] T. P. Treadwell and W. T. Hall, "Analytical Chemistry," Vol. 2, 9th ed, William T. Hall, 1942, pp 93, 297.

[14] J. A. Smythe, *J. Chem. Soc.*, **121**, 1277 (1922); G. Stradnikow and L. Kaschtanow, *Ber.*, **61**, 1389 (1928).

Synthesis of Benzaldehyde-d_1 *via* an Ylide Intermediate[1]

J. CYMERMAN CRAIG AND LOUIS R. KRAY

Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, California 94122

Received June 13, 1967

Aldehydes labeled with deuterium at C-1 have become increasingly valuable in studies of chemical and biochemical reaction mechanisms[2] and methods affording their facile preparation are therefore of wide interest.

Although it has been reported[3] that decarboxylation of aromatic α-keto acids required 13-hr refluxing in the presence of both benzoic anhydride and pyridine, in our hands phenylglyoxylic acid was readily transformed into benzaldehyde (70–74% yield) after 1 hr at 125° in the sole presence of 1.1 molar equiv of a tertiary base in which the nitrogen has the sp^3 configuration. Thus N,N-dimethyl-*p*-toluidine, N-ethylmorpholine, or N,N-dimethylbenzylamine all functioned equally well, whereas when the sp^2-hybridized pyridine was used the yield of aldehyde fell to 30–34%.

These results are consistent with the steric requirements for an intramolecularly hydrogen-bonded intermediate II, formed by nucleophilic attack of the base on the keto carbonyl carbon of the acid I. The intermediate II, or its tautomer IIa, readily loses carbon dioxide to afford the resonance-stabilized ylide III, transformed by loss of base to the aldehyde. Similar ammonium ylides have been reported in the literature.[4]

This mechanism is supported by the following observations. (1) When 2,6-lutidine was used as the base, the yield of aldehyde fell to 1% and more than 90% of phenylglyoxylic acid was recovered. This result is attributable to the additional steric interference between the methyl group of the sp^2-hybridized base and the substrate.[5] (2) Using mesitylglyoxylic acid, under the same conditions under which phenylglyoxylic acid gave benzaldehyde, no decarboxylation took place and

---

[1] Supported by the National Institutes of Health, U. S. Public Health Service (Research Grant HE-5881).

[2] V. E. Althouse, D. M. Feigl, W. A. Sanderson, and H. S. Mosher, *J. Am. Chem. Soc.*, **88**, 3595 (1966), and references cited therein.

[3] T. Cohen and I. H. Song, *ibid.*, **87**, 3780 (1965).

[4] (a) J. Watson and P. Haake, *J. Org. Chem.*, **30**, 1122 (1965); (b) C. K. Ingold and J. A. Jessop, *J. Chem. Soc.*, 2357 (1929); (c) A. W. Johnson, "Ylid Chemistry," Academic Press Inc., New York, N. Y., 1966, pp 253–260.

[5] H. C. Brown, D. Gintis, and H. Podall, *J. Am. Chem. Soc.*, **78**, 5375 (1956).