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Sunlamp-Irradiated Phase-Transfer Catalysis. 1. Cobalt Carbonyl Catalyzed $S_{RN}1$ Carbonylations of Aryl and Vinyl Halides

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Cobalt carbonyl catalyzed carbonylation (1 atm) of aryl and vinyl halides may be easily achieved under phase-transfer-catalysis conditions provided that the reaction medium is irradiated. Irradiation may be achieved by a commercial sunlamp. Most of these reactions may also be performed without organic solvent and in some cases without a phase-transfer agent. Finally, this new, inexpensive carbonylation method allows very efficient synthesis of benzolactams and benzolactones.

Carbonylations of organic halides constitute interesting reactions from two points of view.[1] First, they allow carbon–carbon bond formation with simultaneous introduction of a functional group. Thus, they may allow functionalization of elaborate molecules. Second, if the reactions are easily carried out and the reagents involved are not too expensive, these condensations could be used to transform inexpensive industrial materials to higher commercial value derivatives. For example, they could be of interest in the carbonylation of byproducts provided by industrial halogenations.

Examination of literature data[1] shows that considerable interest has been devoted to this problem and that several solutions have been proposed.

The first kind of reaction consists of carbonylations performed under high CO pressure and at high temperatures in the presence of transition-metal-containing catalysts. This kind of reaction has long been the main method for the carbonylation of aryl halides.[1a]

Reactions performed at lower temperature, with stoechiometric (or higher) amounts of transition-metal carbonyls, have met with some success.[1-3]

A third, and much more interesting, class of reactions consists of carbonylations performed under 1 atm of CO around room temperature in the presence of catalytic or semicatalytic[4] amounts of transition-metal carbonyl species[5] or precursors.[6]

As far as this last class is concerned, it appears that its success strongly depends on the nature of the substrate. Thus, organic halides reactive in S_N2 processes (primary alkyl and a number of secondary alkyl, allyl, and benzyl halides) generally lead to good to fair results.[1a,7,8b] On the contrary, carbonylation of the much less reactive aryl or vinyl halides is difficult to carry out under mild conditions, and only a few systems allow such reactions. Thus, on dismissal of the uncatalytic use of the very hazardous $Ni(CO)_4$,[1a,9] there remain the very efficient reactions performed in the presence of palladium species.[6] The only drawbacks are the high cost of palladium derivatives and, often, the use of phosphines as cocatalysts.

One of the most widespread, low-cost metal carbonyl derivatives is alkali metal (tetracarbonyl)cobaltate.[1a] Carbonylations of aryl halides by means of $MCo(CO)_4$ were unsuccessful[1a,10] up until our discovery that catalytic carbonylation of such halides was achievable by means of a new, heterogeneous reaction medium named "CoCRACO" ($NaH–RONa–Co(OAc)_2–CO$).[11] During investigations performed in order to clarify the mechanism of these carbonylations,[12] we showed for the first time that $Co(CO)_4^-$ may condense with aryl bromides in $S_{RN}1$ processes to yield benzoic acid derivatives.

The results reported by Bunnett et al. concerning photostimulated $S_{RN}1$ condensations,[13] as well as the results reported by Alper concerning the generation of $Co(CO)_4^-$ under phase-transfer-catalysis conditions (PTC),[8] led us to study the photostimulated carbonylations of aryl halides by $Co(CO)_4^-$ under PTC conditions.[14] The first results thus obtained showed a considerable improvement brought about by photostimulation in the field of the carbonylation of organic halides under PTC conditions.

In the present paper, we report complete results concerning the catalytic carbonylation of aryl and vinyl halides. We shall see that irradiation through a Pyrex flask by means of an ordinary commercial sunlamp is sufficient to perform these carbonylations. Moreover, we shall see that, in many cases, very high yields have been obtained even with water as the only reaction solvent.

Results and Discussion

Carbonylation of Aryl Halides. The first and very promising results previously reported[14] were obtained by irradiation (under a slow stream of carbon monoxide) of a stirred mixture of the aryl halide, benzene and 5N aqueous sodium hydroxide in the presence of catalytic amounts of both $Co_2(CO)_8$ and $Bu_4N^+Br^-$ (Scheme I).

Scheme I

$$\mathrm{ArX} \xrightarrow[\mathrm{Co_2(CO)_8,\ Bu_4N^+,Br^-,\ h\nu\ (350\ nm)}]{\mathrm{C_6H_6/aqueous\ 5\ N\ NaOH,\ CO}} \mathrm{ArCOONa}$$

(Triethyl benzyl ammonium halides cannot be used as

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[1] (a) I. Wender and P. Pino, Eds., "Organic Syntheses via Metal Carbonyls", Vol. 1, Wiley-Interscience, New York, 1968; Vol. 2, 1977; (b) J. Falbe, Ed., "Carbon Monoxide in Organic Synthesis", Springer Verlag, West Berlin and Heidelberg, 1970; (c) J. Falbe, Ed., "New synthesis with Carbon Monoxide", Springer Verlag, West Berlin and Heidelberg, 1980.

[2] See for example: J. P. Collman, *Acc. Chem. Res.*, **8**, 342 (1975), and references cited therein.

[3] See for example: E. J. Corey and L. S. Hegedus, *J. Am. Chem. Soc.*, **91**, 1223 (1969).

[4] I.e., carbonylations the yield of which relative to the metal is higher than 100% while they are not truly catalytic.

[5] See for example: M. Nakayama and T. Mizoroki, *Bull. Chem. Soc. Jpn.*, **44**, 508 (1971), and references cited therein.

[6] (a) A. Schoenberg and R. F. Heck, *J. Org. Chem.*, **39**, 3327 (1974), and references cited therein; (b) L. Cassar, M. Foa, and A. Gardano, *J. Organomet. Chem.*, **121**, C55 (1976).

[7] See for example: L. Cassar, G. P. Chiusoli, and F. Guerrieri, *Synthesis*, 509 (1973), and references cited therein.

[8] (a) H. Alper, H. des Abbayes, and D. des Roches, *J. Organomet. Chem.*, **121**, C31 (1976); (b) H. Alper, *Adv. Organomet. Chem.*, **19**, 183 (1981).

[9] L. Cassar and M. Foa, *J. Organomet. Chem.*, **51**, 381 (1973).

[10] R. B. King, *Acc. Chem. Res.*, **3**, 417 (1970), and references cited therein.

[11] J. J. Brunet, C. Sidot, B. Loubinoux, and P. Caubere, *J. Org. Chem.*, **44**, 2199 (1979).

[12] J. J. Brunet, C. Sidot, and P. Caubere, *J. Organomet. Chem.*, **204**, 229 (1980).

[13] J. F. Bunnett, *Acc. Chem. Res.*, **11**, 413 (1978), and references cited therein.

[14] J. J. Brunet, C. Sidot, and P. Caubere, *Tetrahedron Lett.*, **22**, 1013 (1981).

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Table I. $\mathrm{ArX} \xrightarrow[\mathrm{Bu_4N^+,Br^-},\ 65\ ^\circ\mathrm{C},\ h\nu]{\mathrm{Co_2(CO)_8},\ \mathrm{C_6H_6}/5\ \mathrm{N\ NaOH(aq)},\ \mathrm{CO}} \mathrm{ArCOONa}$

ArX[a]	reaction time, h	photostimulation 350 nm	photostimulation sunlamp	ArX[b] recovd, %	ArCOOH[c] (yield, %)
bromobenzene	1.5	+		3	benzoic acid (95)
bromobenzene	1		+	3	benzoic acid (96)
bromobenzene[d]	12	+			benzoic acid (97)
chlorobenzene	13	+		100	
chlorobenzene	24		+	95	benzoic acid (traces)
iodobenzene	1		+		benzoic acid (90)
4-bromotoluene	1		+	2	4-methylbenzoic acid (97)
2-bromotoluene	1.5		+	2	2-methylbenzoic acid (96)
4-bromoanisole	2		+	3	4-methoxybenzoic acid (98)
2-bromoanisole	2		+	3	2-methoxybenzoic acid (50)[e]
4-(bromofluoro)benzene	2		+		4-fluorobenzoic acid (97)
4-(bromochloro)benzene	1	+[f]			4-chlorobenzoic acid (98)[f]
4-bromoacetophenone	4.5		+	3	4-acetylbenzoic acid (90)
4-bromophenol	15	+		80	4-hydroxybenzoic acid (18)
4-(bromonitro)benzene	8		+		4-nitrobenzoic acid (17)[g]
ethyl 4-bromobenzoate	1.5		+		therephthalic acid (97)
2-(bromophenyl)acetamide	20		+		2-(carboxyphenyl)acetic acid (90)
1-bromonaphthalene	4.5		+		1-naphthoic acid (95)
2-bromonaphthalene	1.5		+		2-naphthoic acid (97)

[a] ArX, 20 mmol; $\mathrm{Co_2(CO)_8}$, 1 mmol; $\mathrm{Bu_4N^+Br^-}$, 2 mmol; $\mathrm{C_6H_6}$, 25 mL; aqueous NaOH, 50 mL. [b] Determined by GLC analysis with internal standards. [c] Isolated yields. [d] Reaction performed at 35 °C. [e] 47% anisole formation was observed (GLC analysis). [f] The same result was obtained with the sunlamp. [g] 17% nitrobenzene formation was observed (GLC analysis).

phase transfer agent. Indeed, we have shown that, under the conditions used, these ammonium halides were carbonylated to phenyl acetic acid).[15]

Irradiation was achieved through a Pyrex reaction flask placed inside a Rayonet apparatus equipped with 350-nm lamps. With the goal of large-scale preparations in mind, we wondered whether such reactions could not be performed with a much less sophisticated apparatus.

In their pioneering work on $\mathrm{S_{RN}1}$ reactions, Bunnett et al. used a 380-W tungsten lamp to irradiate condensations performed in liquid ammonia.[16] In the present work, replacing the 350-nm device by a 500-W tungsten lamp only led to slow carbonylation of bromobenzene (no carbonylation at all occured in the absence of any kind of irradiation). Thus we turned toward an inexpensive, commercial sunlamp (characteristics given in the Experimental Section). Exploratory experiments conducted with bromobenzene showed that, placed about 30 cm from the Pyrex reaction flask, this kind of lamp was at least as efficient as the 16 (350-nm) lamps of the Rayonet apparatus. Moreover, although the lamp used was only 6 cm long by itself, it was possible to irradiate simultaneously three reaction flasks.

The results obtained with the sunlamp have been grouped in Table I where we have also reported some results obtained with the 350-nm device. These results deserve some comments.

First of all, it is clear that irradiation with the sunlamp resulted in the same yields as irradiation with the 350-nm lamps and that reaction times were either the same or even shorter.

Under the above conditions, chlorobenzene was not carbonylated after 13 h of reaction. This lack of reactivity has been used to perform the selective carbonylation of *p*-chlorobromobenzene to *p*-chlorobenzoic acid of very high purity.

Except in three cases, acid yields were nearly quantitative, and the only side product formed was a small amount of the reduced derivative. More accurate study of the behavior of *o*-bromoanisole and *p*-bromonitrobenzene showed that the unsatisfactory results obtained were due to intensive reduction and destruction of the substrate, respectively. On the contrary, *p*-bromophenol exhibited only a low reaction rate with little or no reduction to phenol. Thus, it could be expected that, under more appropriate conditions, it should be possible to obtain better results. We shall see later that this expectation has been verified.

Then, always with the potentiality of large-scale operations in mind, we wondered whether the industrialy undesirable benzene could not be replaced by a more harmless solvent and $\mathrm{Co_2(CO)_8}$ by a simpler cobalt derivative.

Reactions performed on bromobenzene showed that toluene or a commercial mixture of xylenes could be used as the solvent (96% and 93% benzoic acid yields, respectively) with the same reaction time as when benzene was used. Interestingly, even 1,2-dichlorobenzene (a classical solvent for PTC[17]) may be used (90% benzoic acid yield) although a longer reaction time (2.5 h) was necessary.

As to the replacement of $\mathrm{Co_2(CO)_8}$ by a simpler cobalt derivative, we turned toward an old preparation of $\mathrm{KCo(CO)_4}$ in aqueous medium, starting from $\mathrm{Co(NO_3)_2}$, KCN, and aqueous potassium hydroxide.[18] Use of 2 mmol (see Experimental Section) of $\mathrm{KCo(CO)_4}$ prepared by this method instead of 1 mmol of $\mathrm{Co_2(CO)_8}$ allowed the carbonylation of bromobenzene to benzoic acid in the same yield and in the same reaction time (in this case a very small amount of benzonitrile was detected by GLC analysis). Thus this preparation constitutes an interesting alternative which avoids the use of $\mathrm{Co_2(CO)_8}$. We also tried to prepare $\mathrm{KCo(CO)_4}$ directly in the reaction flask for carbonylation by mixing together both the reagents needed for the generation of $\mathrm{KCo(CO)_4}$ and those needed for the carbonylation. As may be seen from Scheme II, carbonylation did occur under these conditions, but longer reaction times were required.

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(15) J. J. Brunet, C. Sidot, and P. Caubere, *J. Org. Chem.*, in press.

(16) See for example: R. A. Rossi and J. F. Bunnett, *J. Org. Chem.*, **38**, 1407 (1973).

(17) See for example: C. M. Starks and C. Liotta, "Phase Transfer Catalysis, Principles and Techniques", Academic Press, London and New York, 1978.

(18) A. A. Blanchard and P. Gilmont, *J. Am. Chem. Soc.*, **62**, 1192 (1940).

Table II. $4\text{-}ZC_6H_4Br \xrightarrow[\text{sunlamp}]{Co_2(CO)_8,\ 5\ N\ NaOH(aq),\ 65\ ^\circ C^a} 4\text{-}ZC_6H_4COONa$

reaction medium	Z	reaction time, h	acid isolated yield, %	recovd starting matl, %
C_6H_6/aqueous 5 N NaOH/Bu_4N^+,Br^- [b]	H	1	96	3[d]
	MeO	2	98	3[d]
	OH	15	18	80
aqueous 5 N NaOH/Bu_4N^+,Br^- [c]	H	2	95	5[d]
	MeO	2.5	92	5[d]
	OH	15	35-40	60-65
aqueous 5 N NaOH	H	2	45	50[d]
	MeO	5	35	62[d]
	OH	15	90	5

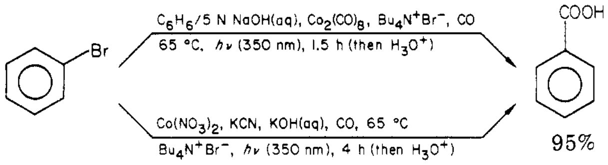
[a] Ratio of aryl halide/$Co_2(CO)_8$ of 20/1 (mmol). In all cases, 50 mL of aqueous 5 N NaOH was used. [b] C_6H_6, 25 mL; Bu_4N^+,Br^-, 2 mmol. [c] Bu_4N^+,Br^-, 2 mmol. [d] Determined by GLC analysis with internal standards.

Table III. Carbonylation of Aryl Chlorides[a]

aryl halide	conditions[b] (reaction time, h)	acid	isolated yield, %
C_6H_5Cl	A (24)	C_6H_5COOH	traces[c]
$4\text{-}ClC_6H_4OH$	B (15)		c
	C (15)		c
$4\text{-}ClC_6H_4COOH$	B (8)	$4\text{-}(COOH)C_6H_4COOH$	98
	C (8)	$4\text{-}(COOH)C_6H_4COOH$	98
$4\text{-}ClC_6H_4CH_2COOH$	C (15)	$4\text{-}(COOH)C_6H_4CH_2COOH$	80[d]

[a] Reactions performed at 65 °C with the following reactants: aryl halide, 20 mmol; $Co_2(CO)_8$, 1 mmol. [b] Condition A: PTC (C_6H_6, 25 mL; aqueous 5 N NaOH, 50 mL) with a $Bu_4N^+,Br^-/Co_2(CO)_8$ ratio of 2. Condition B: aqueous 5 N NaOH (50 mL), with a $Bu_4N^+,Br^-/Co_2(CO)_8$ ratio of 2. Condition C: aqueous 5 N NaOH (50 mL), without ammonium salt. [c] 98% recovered starting material. [d] 20% recovered starting material, as determined by ^1H NMR of the mixture of the methyl esters obtained by reaction of the acids with diazomethane.

Scheme II



This observation may be explained by the fact that generation of $Co(CO)_4^-$ from $Co(NO_3)_2$ is slower than from $Co_2(CO)_8$. However, it is clear that good results may be obtained without the use of $Co_2(CO)_8$ as starting material.

Continuing in the simplification of experimental conditions, we tried to determine whether the organic solvent was necessary to perform these reactions and whether the phase-transfer catalyst was still necessary in the absence of organic solvent. The results obtained with three substrates have been summarized in Table II (where results obtained by using benzene have been reported for comparison). Some very interesting points emerge.

With Z = H or MeO, it appears that, in the presence of the ammonium salt, carbonylations may be performed without benzene as the organic solvent (note, however, the longer reaction time). In fact, in these experiments, the organic phase was constituted of the aryl halide itself. Finally, if the ammonium salt was omitted, carbonylation still occurred but the reaction rate was slowed down.

More interesting and intriguing results were observed for Z = OH. Indeed, better carbonylation yields were obtained in the absence of benzene. This observation may be explained by the fact that, under PTC conditions, the catalyst $Co(CO)_4^-$ remains in the organic layer[19] while bromophenol remains, as a sodium salt, in the aqueous phase. Thus, carbonylation cannot easily take place. In aqueous sodium hydroxide, both the substrate and the catalyst remain in the same phase, and better results are obtained. However, what cannot be easily explained is that, in the absence of ammonium salt, carbonylation took place in aqueous sodium hydroxide at a still higher reaction rate, thus leading to excellent carbonylation yields in 15 h.

So, it clearly appears that the carbonylations may be performed under very simple and inexpensive PTC conditions, for example, to carry out continuous preparations. Alternatively, the organic solvent may be omitted provided that longer reaction times are allowed.

The results obtained for the carbonylation of *p*-bromophenol led us to examine the behavior of acid aryl chlorides in the hope of determining conditions allowing the carbonylation of the unreactive chloro compounds. As may be seen from Table III, *p*-chlorophenol was quantitatively recovered after 15 h under either condition B or C (for definitions, see the footnotes of Table III). On the contrary, *p*-chlorobenzoic acid and (*p*-chlorophenyl)acetic acid were easily carbonylated in aqueous sodium hydroxide, even in the absence of ammonium salt.

One of the most interesting applications of the carbonylation of aryl halides is the synthesis of benzolactams and lactones starting from aryl halides bearing amino or hydroxy groups on a side chain α to the halogen. Such carbonylations have already been performed[20,21] by using the palladium-based carbonylation reported by Heck.[6a]

Using the experimental conditions described above (photostimulated PTC), we have performed some cyclizations of this type. The main results are summarized in Table IV. They clearly show that the photostimulated carbonylations reported in this work are particularly well suited for the synthesis of lactones and lactams.

Separating the two phases of the reaction medium showed that lactams were present in the organic phase, and

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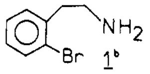
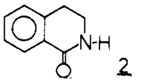
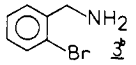
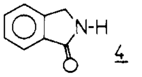
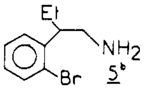
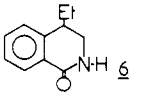
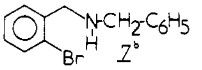
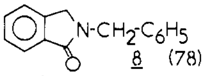
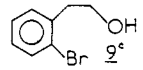
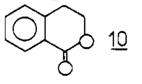
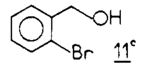
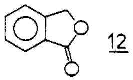
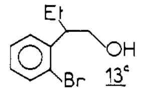
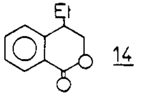
(19) H. des Abbayes and A. Buloup, *Tetrahedron Lett.*, 21, 4343 (1980).

(20) M. Mori, K. Chiba and Y. Ban, *J. Org. Chem.*, 43, 1684 (1978).

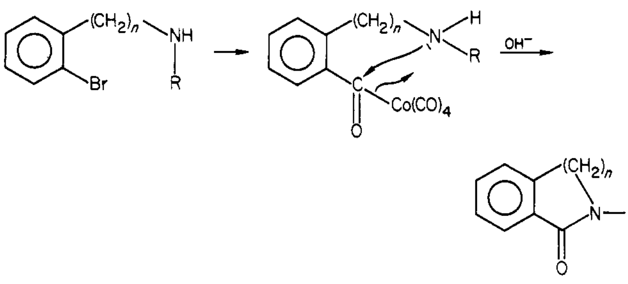
(21) A. Cowell and J. K. Stille, *J. Am. Chem. Soc.*, 102, 4193 (1980).

Table IV. Synthesis of Benzolactams and Benzolactones[a]

aryl halide	product (yield, %)
 1[b]	 2 (72)
 3[b]	 4 (60)
 5[b]	 6 (82)
 7[b]	 8 (78)
 9[c]	 10 (95)
 11[c]	 12 (95)
 13[c]	 14 (92)

[a] Reactions were performed at 65 °C in a two-phase system [C_6H_6 (25 mL)/aqueous 5 N NaOH (50 mL)] with the following reactants: ratio of aryl halide/$Co_2(CO)_8$/$Bu_4N^+Br^-$ of 20/1/2 (mmol). Photostimulation was achieved with the sunlamp. [b] Reaction time 5.5 h. [c] Reaction time 2.5 h.

Scheme III



this led us to conclude that these lactams were formed in situ. In other words, the classical condensation of the nucleophile with the aroylcobalt carbonyl easily takes place (Scheme III).

When the amine function was replaced by a hydroxy, the same reaction may take place. However, the resulting lactones are much too sensitive to the basic medium to remain as such. Thus, they were present in the reaction medium in the form of hydroxyalkylbenzoic acid salts, and the lactones themselves were formed during the acidic workup.

In any case, the results obtained compare very favorably with those performed with palladium species, particularly in the case of lactams in which the nitrogen atom has no substituent.[20] Indeed, the present method is much less expensive, the reactions are carried out under milder conditions, and yields are of the same magnitude (and often higher) than those obtained with palladium species.

Carbonylation of Vinyl Halides. Bunnett et al. have reported that vinyl halides, although less reactive than aryl halides, may condense with nucleophiles in $S_{RN}1$ processes.[22] Thus, it was of theoretical as well as practical interest to examine the behavior of such halides toward $Co(CO)_4^-$ under the conditions reported above.

Table V. Carbonylation of Vinyl Halides[a]

vinyl halide	reaction time, h	product (yield, %)
1-bromocyclooctene	4.5	1-cyclooctenecarboxylic acid (97)
1-bromocyclohexene	2.5	1-cyclohexenecarboxylic acid (98)
1-chlorocyclohexene	2.5	1-cyclohexenecarboxylic acid (97)
3,3-dimethyl 2-chlorobut-1-ene	2	2-*tert*-butyl acrylic acid (95)
trans-β-bromostyrene	8	*trans*-cinnamic acid (62), *trans*-β-bromostyrene (35)
	15	*trans*-cinnamic acid (85), *trans*-β-bromostyrene (5)
cis-β-bromostyrene	8	*cis*-cinnamic acid (35),[b] *trans*-cinnamic acid (35),[b] *cis*-β-bromostyrene (30)
	15	*cis*-cinnamic acid (38),[b] *trans*-cinnamic acid (42),[b] *cis*-β-bromostyrene (5)

[a] Reactions were performed at 65 °C in a two-phases system (C_6H_6, 25 mL; aqueous 5 N NaOH, 50 mL) using the following: ratio of vinyl halide/$Co_2(CO)_8$/Bu_4N^+,Br^- of 20/1/2 (mmol). Photostimulation was assured by the sunlamp. [b] Determined by ^1H NMR.

As may be seen from Table V, it was found that vinyl bromides and chlorides may be carbonylated to afford the corresponding α,β-unsaturated acids in high yield. (Vinyl chloride was also shown to undergo carbonylation under these conditions, but yields were not optimized.) Concerning the carbonylation of β-bromostyrenes, the trans derivative led to pure *trans*-cinnamic acid while the cis isomer led to a mixture of *cis*- and *trans*-cinnamic acids. Stopping each reaction after 8 h showed that no isomerization of the starting bromide had occured. Control experiments performed under simulated reaction conditions indicated that *cis*-cinnamic acid (as sodium salt) was isomerized to only 15% after 15 h of irradiation at 65 °C. Furthermore, stopping the carbonylation of *cis*-β-bromostyrene after 15% conversion led to a mixture of cinnamic acids in nearly equal amounts (^1H NMR). Thus it appears that the carbonylation itself is not stereospecific while we could not determine whether the isomerization occurs by isomerization of the radical anion (or of the vinyl radical, during $S_{RN}1$ condensation) or by isomerization of the intermediate cinnamoylcobalt carbonyl species.

It has also been shown that these reactions may be performed without an organic solvent. Thus, carbonylation of 1-bromocyclooctene in aqueous sodium hydroxide in the presence of Bu_4N^+, Br^- led to the corresponding acid in 92% yield after 5 h. Thus it seems that, as for aryl halides, these carbonylations may be performed by using the substrate as the organic solvent.

Mechanistic Considerations. The photostimulated carbonylations described above seem to occur via $S_{RN}1$ condensation of $Co(CO)_4^-$ with aryl or vinyl halides, and we have previously proposed a detailed mechanism for this kind of carbonylations.[12] However, the question of the initiation step remains unanswered. Although no experiments have been performed to get more insight into this problem, the results obtained with *p*-bromophenol (vide supra) allow the proposal of some hypotheses.

On consideration of the UV absorption spectra of the substrates and the energy and the number of photons able to reach them under the conditions used, photolysis of aryl bromides may be ruled out as the initiation step. The other possibility, according to Bunnett's hypothesis[13,16] is the formation of charge-transfer complexes between ArX and $Co(CO)_4^-$,M^+ from which photostimulation leads to

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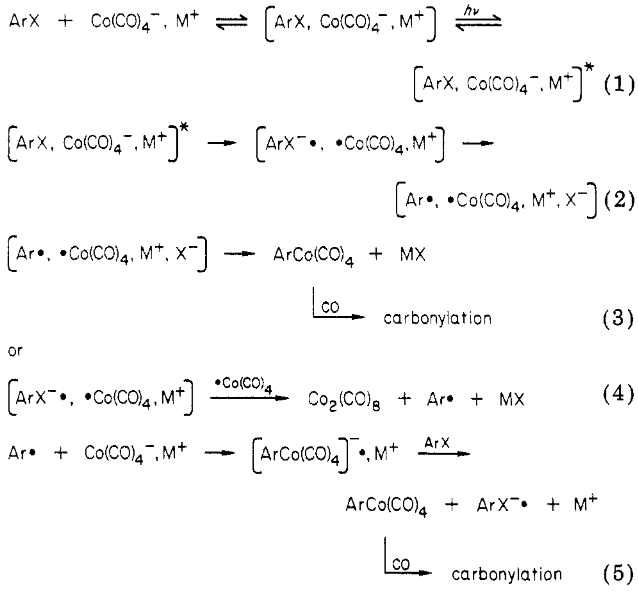
(22) J. F. Bunnett, X. Creary, and J. E. Sundberg, *J. Org. Chem.*, 41, 1707 (1976).

Scheme IV



the initial step of the condensation. The results obtained with *p*-bromophenol (vide supra) lead us to favor this explanation.

Indeed, during $S_{RN}1$ condensations of nitrile or ketone enolates with 1-bromo-2-naphthoxide, Rossi observed very low condensation yields with formation of large amounts of 2-naphthol.[23] The explanation was that the photostimulated electron transfer from the nucleophile to the substrate took place, followed by loss of Br^-, thus leading to a radical. However, the low electrophilicity of this radical, bearing the electron-releasing group, impedes the condensation of the nucleophile and thus favors abstraction of a hydrogen atom to give the reduction product.

In the present work, when the carbonylation of *p*-bromophenol takes place in low yields, the remaining starting aryl bromide is recovered nearly quantitatively. Thus, according to the hypothesis of Rossi[23] it must be concluded that, at least under PTC conditions or in aqueous sodium hydroxide, $Co(CO)_4^-$ is a poorer electron-donating species than enolates. On the other hand, $Co(CO)_4^-$ is known as a poor nucleophile[10] (both properties are, of course, correlated). Thus, the only expected product should be the reduction product. The fact that the contrary was observed strongly supports the hypothesis that the aryl radical formed is strongly held inside a cobalt carbonyl containing complex (Scheme IV), so that the radical would exhibit a low propensity for escaping to abstract a hydrogen atom.

Of course, the possibility that 4 and 5 take place cannot be dismissed. However, in the case of *p*-bromophenol, this possibility appears highly improbable as no reduction product was observed.

Conclusion

In conclusion, cobalt carbonyl catalyzed carbonylations under irradiated PTC conditions open a new field of interesting applications for the functionalization of aryl and vinyl halides. Their applicability has been clearly evidenced for the synthesis of benzolactams and benzolactones.

From a practical point of view, this new technique is very easy to carry out, is inexpensive, and may be used for large-scale operations. However, the most important feature of this work is probably the finding that carbonyl metalates may react in $S_{RN}1$ processes. Thus, this new kind of reaction has to be extended to other metalates, and we are presently studying the possibilities of such reactions for the functionalization of organic substrates.

Experimental Section

Materials. Tetrabutylammonium bromide, dicobalt octacarbonyl, and cobalt nitrate were purchased from Fluka and were used without further purification. Carbon monoxide N20 (L'Air Liquide) was used. Starting materials for the synthesis of lactams and lactones were prepared by standard procedures. **1** was obtained from *o*-bromobenzyl bromide via 2-(2-bromophenyl)ethyl bromide[24] followed by Gabriel synthesis in DMF.[25] For **1**: colorless liquid; NMR (neat) δ 1.45 (s, 2 H, NH_2), 2.85 (s, 4 H), 6.8–7.3 (m, 3 H aromatic), 7.4–7.65 (m, 1 H, aromatic). **3** was prepared from *o*-bromobenzyl bromide by Gabriel synthesis:[25] colorless liquid; NMR ($CDCl_3$) δ 1.6 (s, 2 H, NH_2), 3.85 (s, 2 H), 7.0–7.7 (m, 4 H, aromatic). **5** was prepared from 2-bromobenzyl bromide via (*o*-bromophenyl)acetonitrile followed by alkylation[26] and by following the same procedure as for **1**. For **5**: colorless liquid; NMR ($CDCl_3$) δ 0.85 (t, 3 H), 1.35 (s, 2 H, NH_2), 1.3–2.0 (m, 2 H), 2.8–3.6 (m, 3 H), 6.95–7.45 (m, 3 H, aromatic), 7.5–7.8 (m, 1 H, aromatic). **7** was prepared from *o*-bromobenzaldehyde.[20] **9** was prepared from *o*-bromobenzyl bromide:[24] colorless liquid; NMR ($CDCl_3$) δ 2.25 (s, 1 H, OH), 2.95 (t, 2 H), 3.8 (t, 2 H), 7.0–7.5 (m, 3 H, aromatic), 7.5–7.8 (m, 1 H, aromatic). **11** was obtained by hydrolysis of *o*-bromobenzyl bromide: mp 80 °C; NMR ($CDCl_3$) δ 2.25 (m, 1 H, OH), 4.7 (s, 2 H), 7.0–7.8 (m, 4 H, aromatic). **13** was prepared from *o*-bromobenzyl bromide via (*o*-bromophenyl)acetonitrile followed by alkylation[26] and then the procedure described in ref 24: colorless liquid; NMR ($CDCl_3$) δ 0.85 (t, 3 H), 1.2–2.0 (m, 3 H), 3.0–3.9 (m, 3 H), 6.9–7.4 (m, 3 H, aromatic), 7.5–7.8 (m, 1 H, aromatic).

General Methods. All melting points are uncorrected. GLC analyses were carried out on a Girdel 300 apparatus equipped with 5-m (15% SE-30 or 10% UCON 50 HB 2000) columns. IR spectra were recorded with a Perkin-Elmer spectrophotometer (Model 580 B). NMR spectra were recorded on a Perkin-Elmer R 12 B instrument with Me_4Si as an internal standard. The sunlamp used was purchased from Philips. It was equipped with a Philips 13178 HPQ 125-W lamp (main emissions at 300, 315, 365, 405, and 435 nm).

Carbonylation of Aryl Halides (Table I). To a 250-mL Pyrex flask were added benzene (25 mL), $Co_2(CO)_8$ (1 mmol), aqueous 5 N sodium hydroxide (50 mL), tetrabutylammonium bromide (2 mmol), and the aryl halide (20 mmol). The reaction mixture was heated to 65 °C under a slow stream of carbon monoxide. (Heating was assured by means of the IR device of the sunlamp.) Irradiation was achieved with the sunlamp placed about 30 cm from the reaction flask. After the mixtures were stirred under these conditions for the times indicated in Table I, a classical acidic workup afforded the expected acids in high purity which were identified by comparison with authentic samples (melting point, IR, NMR).

These reactions may also be performed (see text) by replacing $Co_2(CO)_8$ by a titrated aqueous solution of $KCo(CO)_4$ (2 mmol) prepared according to ref 18. Alternatively, the carbonylation may be carried out by mixing together (see Scheme II) $Co(NO_3)_2 \cdot 6H_2O$ (2 mmol), KCN (2 mmol), $Bu_4N^+Br^-$ (2 mmol), and the aryl halide in a two-phase system consisting of C_6H_6 (25 mL) and aqueous 5N KOH (50 mL) under carbon monoxide.

Carbonylation of Aryl Halides (Table II). These carbonylations were performed by using $Co_2(CO)_8$ as a catalyst precursor and were conducted either as described above or in the absence of benzene (conditions described in the footnotes of Table II).

Carbonylation of Aryl Chlorides (Table III). These reactions were carried out either as described above or in the absence

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[23] R. A. Rossi, R. H. de Rossi, and A. F. Lopez, *J. Org. Chem.*, **41**, 3371 (1976).

[24] F. Bickelhaupt, K. Stach, and M. Thiel, *Chem. Ber.*, **98**, 685 (1965).

[25] J. C. Sheehan and W. A. Bolhofer, *J. Am. Chem. Soc.*, **72**, 2786 (1950).

[26] M. Makosza and A. Jonczyk, *Org. Synth.*, **55**, 91 (1976).

of benzene, with $Co_2(CO)_8$ as catalyst precursor. Reactant ratios and reaction mediums are given in the footnotes of Table III.

Synthesis of Benzolactams and Benzolactones (Table IV). Carbonylations were conducted as described above in a two-phase system: C_6H_6/NaOH(aq) (reactant ratios are given in the footnotes of Table IV). At the end of the reaction, lactams were present in the organic phase which was washed several times with water and dried over $MgSO_4$. On the contrary, isolation of lactones was achieved by acidification of the aqueous phase followed by a classical workup and drying over $MgSO_4$. All cyclized compounds were purified by column chromatography on a short silica gel column or by recrystallization. Satisfactory analytical data (±0.4% for C, H, and N) were obtained for all new compounds listed in Table IV. They were characterized by comparison with literature data (melting point, IR, NMR) or on the basis of their spectroscopic properties (IR, NMR).

Benzolactam 2: colorless oil; IR (film) ν_{max} 3250, 1665 (s), 1605, 1575 cm^{-1}; NMR ($CDCl_3$) δ 2.90 (t, 2 H), 3.3–3.7 (m, 2 H), 7.0–7.6 (m, 3 H, aromatic), 7.7–8.4 (m, 2 H, aromatic and NH).

Benzolactam 4: mp 151 °C (lit.[27] mp 150 °C); IR (Nujol) ν_{max} 3220, 1685 cm^{-1}; NMR (C_3D_6O) δ 4.6 (s, 2 H), 7.5–8.1 (m, 5 H, aromatic and NH).

Benzolactam 6: colorless liquid; IR (film) ν_{max} 3220, 1670, 1605, 1575 cm^{-1}; NMR ($CDCl_3$) δ 0.9 (t, 3 H), 1.3–2.0 (m, 2 H), 2.5–3.0 (m, 1 H), 3.1–3.9 (m, 2 H), 7.1–7.9 (m, 3 H, aromatic), 7.8–8.3 (m, 2 H, aromatic + NH).

Benzolactam 8: mp 91 °C (lit.[21] mp 90–91 °C); IR (Nujol) ν_{max} 1680, 1620, 1600 cm^{-1}; NMR ($CDCl_3$) δ 4.25 (s, 2 H), 4.80 (s, 2 H), 7.1–7.6 (m, 8 H, aromatic), 7.7–8.1 (m, 1 H, aromatic).

Benzolactone 10: IR (film) 1720 cm^{-1} (large); NMR ($CDCl_3$) δ 3.0 (t, 2 H), 4.5 (t, 2 H), 7.1–7.8 (m, 3 H, aromatic), 7.8–8.3 (1 H, aromatic).

Benzolactone 12: mp 72–73 °C (petroleum ether); (lit.[28] mp 73 °C); IR (CCl_4) ν_{max} 1768 cm^{-1}; NMR ($CDCl_3$) δ 5.35 (s, 2 H), 7.4–7.8 (m, 3 H, aromatic), 7.8–8.2 (m, 1 H, aromatic).

Benzolactone 14: colorless liquid; IR (film) ν_{max} 1730 cm^{-1}; NMR ($CDCl_3$) δ 1.0 (t, 3 H), 1.5–2.1 (m, 2 H), 2.6–3.1 (m, 1 H), 4.5 (d, 2 H), 7.2–7.8 (m, 3 H, aromatic), 8.0–8.4 (m, 1 H, aromatic).

Carbonylation of Vinyl Halides (Table V). Carbonylation of vinyl halides was carried out in a two-phase system [C_6H_6/NaOH(aq)] by using the general procedure described above for aryl halides. Reactant ratios are given in the footnotes of Table V. All isolated acids were identified by comparison (IR, NMR) with authentic samples, either commercial or prepared by standard methods.

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Registry No. **1**, 65185-58-2; **2**, 1196-38-9; **3**, 3959-05-5; **4**, 480-91-1; **5**, 67932-62-1; **6**, 55150-61-3; **7**, 65185-56-0; **8**, 13380-32-0; **9**, 1074-16-4; **10**, 4702-34-5; **11**, 18982-54-2; **12**, 87-41-2; **13**, 85029-25-0; **14**, 85029-26-1; bromobenzene, 108-86-1; chlorobenzene, 108-90-7; iodobenzene, 591-50-4; 4-bromotoluene, 106-38-7; 2-bromotoluene, 95-46-5; 4-bromoanisole, 104-92-7; 2-bromoanisole, 578-57-4; 4-bromofluorobenzene, 460-00-4; 4-bromochlorobenzene, 106-39-8; 4-bromoacetophenone, 99-90-1; 4-bromonitrobenzene, 586-78-7; ethyl 4-bromobenzoate, 5798-75-4; (2-bromophenyl)acetamide, 65999-53-3; 1-bromonaphthalene, 90-11-9; 2-bromonaphthalene, 580-13-2; 4-chlorophenol, 106-48-9; 4-chlorobenzoic acid, 74-11-3; 4-chlorobenzeneacetic acid, 1878-66-6; 1-bromocyclooctene, 4103-11-1; 1-bromocyclohexene, 2044-08-8; 1-chlorocyclohexene, 930-66-5; 3,3-dimethyl-2-chlorobut-1-ene, 27843-27-2; (*E*)-β-bromostyrene, 588-72-7; (*Z*)-β-bromostyrene, 588-73-8; 4-bromophenol, 106-41-2; benzoic acid, 65-85-0; 4-methylbenzoic acid, 99-94-5; 2-methylbenzoic acid, 118-90-1; 4-methoxybenzoic acid, 100-09-4; 2-methoxybenzoic acid, 579-75-9; 4-fluorobenzoic acid, 456-22-4; 4-acetylbenzoic acid, 586-89-0; 4-hydroxybenzoic acid, 99-96-7; 4-nitrobenzoic acid, 62-23-7; terephthalic acid, 100-21-0; (2-carboxyphenyl)acetic acid, 89-51-0; 1-naphthoic acid, 86-55-5; 2-naphthoic acid, 93-09-4; 1-cyclooctenecarboxylic acid, 4103-09-7; 1-cyclohexenecarboxylic acid, 636-82-8; 2-*tert*-butylacrylic acid, 4423-82-9; *trans*-cinnamic acid, 140-10-3; *cis*-cinnamic acid, 102-94-3; dicobaltoctacarbonyl, 10210-68-1; tetrabutylammonium bromide, 1643-19-2.

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Solvolytic Behavior of 1-Acetoxy-4-(acetoxyimino)-1,4-dihydroquinoline, a Model for the Activated Form of the Carcinogenic 4-Nitroquinoline *N*-Oxide[†]

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The solvolytic behavior of the title compound **3**, a model for the activated form of the bifunctional carcinogenic 4-nitroquinoline 1-oxide (**1**) has been explored to find conditions for selective deacylation to the corresponding monoacetyl derivatives **4** and **5**. At pH 7, in a water–methanol mixture, the solvolysis is rapid ($1/2\ \tau = 6$ min), quite unselective, and leads to a complex mixture. At basic pH, the 1-acetyl group is selectively removed to give the 4-monoacetyl derivative **4**, which immediately undergoes further reaction. Under highly acidic conditions, both monoacyl compounds **4** and **5** are formed. However, due to their different reactivity, **5** can be separated from **4** as its crystalline hydrochloride.

4-Nitroquinoline 1-oxide (**1**, 4-NQO) is a powerful carcinogenic compound whose mode of action at the molecular level is not fully understood.[1] A number of biological studies have led to the conclusion that the first activation step in vivo is the reduction to the (hydroxyamino)quinoline 1-oxide **2**[2] (which exists mainly as its hydroxyimino tautomer **2b**).[3] This compound is subsequently converted to a metabolite(s) which is (are) able to bind covalently to nucleophilic sites of nucleic acid bases. Diacetate **3** and monoacetate **4** have been proposed as

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[†] Dedicated to Professor Edgar Lederer on the occasion of his 75th birthday.

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