Palladium-Catalyzed Amidation of Aryl, Heterocyclic, and Vinylic Halides

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Aryl, heterocyclic, and vinylic halides react with CO and primary or secondary amines with a dihalobistriphenylphosphinepalladium(II) catalyst at 100° or below and 1 atm pressure to form substituted amines in good yields. If the amines are weakly basic, a strongly basic tertiary amine must also be present in stoichiometric amounts. The reaction is highly stereospecific with cis and trans vinylic halides.

The preceding paper reports a new synthesis of esters under mild conditions from aryl, benzyl, or vinylic halides, carbon monoxide, a tertiary amine, an alcohol, and a catalytic amount of various triphenylphosphine–palladium salt complexes.[1] In this paper we report an analogous reaction which produces primary or secondary amides when the above reaction is carried out with a primary or secondary amine in place of the alcohol.

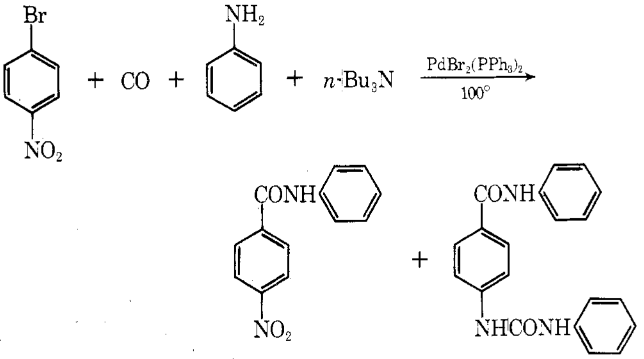
$$\mathrm{RX + CO + R'NH_2 + R_3''N \xrightarrow{PdX_2[P(C_6H_5)_3]_2} RCONHR' + R_3''NH^+X^-}$$

Results and Discussion

A variety of aryl, heterocyclic, and vinylic bromides and iodides have been treated with carbon monoxide at atmospheric pressure, a primary or secondary amine, and a tertiary amine in the presence of about 1.5 mol % $PdX_2[P(C_6H_5)_3]_2$ as catalyst at 60–100°. 2-Chloropropene was also allowed to react but under 600 psi pressure. The amides formed in these reactions are listed in Table I along with the yields and reaction conditions. The yields of isolated purified amides ranged from 57 to 94%. The nmr data for the products are given in Table II, which will appear in the microfilm edition of this journal. See paragraph at end of paper regarding supplementary material. The reactions proceeded more rapidly than the related ester synthesis judging by the half-lives ($T_{1/2}$) observed. (The approximate half-lives were the times required for half of the theoretical amount of carbon monoxide to be absorbed). For example, bromobenzene reacts under the above conditions about 17 times faster with benzylamine to form *N*-benzylbenzamide than it does with *n*-butyl alcohol to form *n*-butyl benzoate. The amidation reaction also shows improved stereospecificity over the carboalkoxylation reaction with cis and trans vinylic halides. The reactions proceeded with high specificity producing amides with retained configuration. We were unable to find more than traces of isomerized products in the reaction mixtures. The amides were nicely crystalline compounds in general and were easily purified by recrystallization.

A tertiary amine was generally added with the primary or secondary amine to neutralize the hydrogen halide formed in the reaction. If the primary or secondary amine was a strong enough base the tertiary amine was not required. Aniline for example does not react without the tertiary amine while pyrrolidine does.

The N-phenylamidation of 4-nitrobromobenzene was complicated by the fact that reduction of the nitro group catalyzed by the palladium also occurred forming an *N*-phenylurea group from the nitro group, CO, and aniline. The urea formation may proceed by way of an isocyanate[2] or an amine.[3] In any case, the urea formation is apparently slower than the amidation and by stopping the reaction when approximately the theoretical amount of CO for formation of the amide is absorbed the *N*-phenyl-4-nitrobenzamide was isolated in 57% yield. Allowing the reaction to proceed until 1.57 mol of CO were absorbed, there was isolated 33% of the *N*-phenylamide of 4-carboxydiphenylurea in addition to 10% of the nitroamide. The yield of the urea probably could be improved if more aniline had been used. This reaction is being investigated as a possible method for preparing other unsymmetrical urea derivatives.



cis-2-Bromostyrene was treated with CO and pyrrolidine under the usual conditions but only about half of the theoretical amount of CO was absorbed. In addition to *trans*-*N*-cinnamoylpyrrolidine, isolated in 6% yield (probably formed from the 8% of *trans*-2-bromostyrene present in the starting material), *cis*-1,4-diphenyl-1-buten-3-yne was isolated in 46% yield. The last product is likely produced by a reaction of the intermediate *cis*-styrylpalladium complex with phenylacetylene and then the adduct eliminating metal hydride (a trans elimination is required). The phenylacetylene is probably formed in this reaction and not others because the relatively unhindered, strong base, pyrrolidine causes a trans dehydrobromination of the *cis*-2-bromostyrene. The liquid cis styrylacetylene isomer obtained (J = 12 Hz for the vinylic hydrogens) isomerized slowly on standing in the light at room temperature to the known solid trans isomer, mp 96.5–97° [4] (J = 18 Hz for the vinylic hydrogens). The only other material isolated from the reaction mixture was a viscous oil which by its nmr and ir spectra appeared to be a polymeric mixture of aromatic carbonyl compounds.

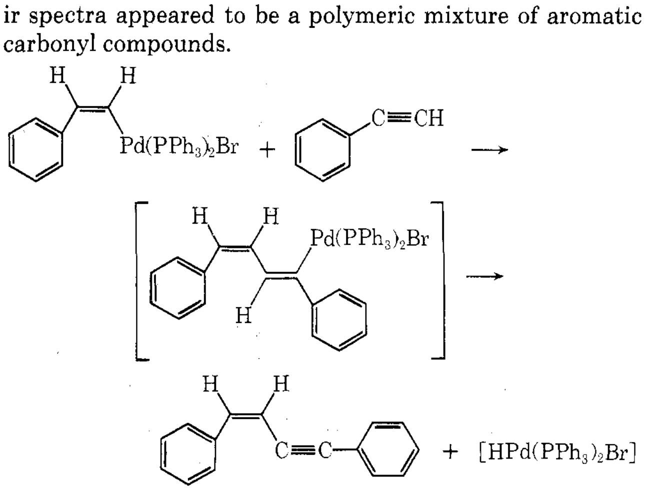
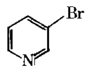
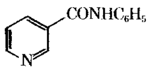
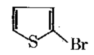
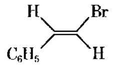
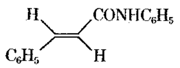
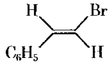
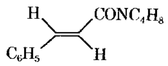
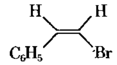
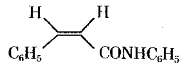
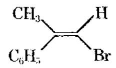
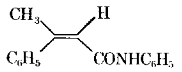
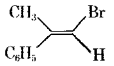
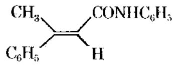
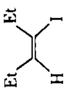
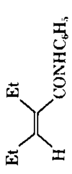
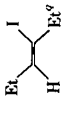
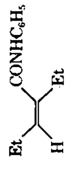
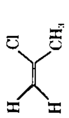
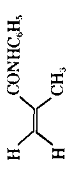
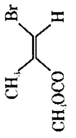
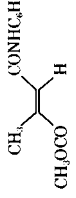


Table I
Amidation of Aryl and Vinylic Halides[a]

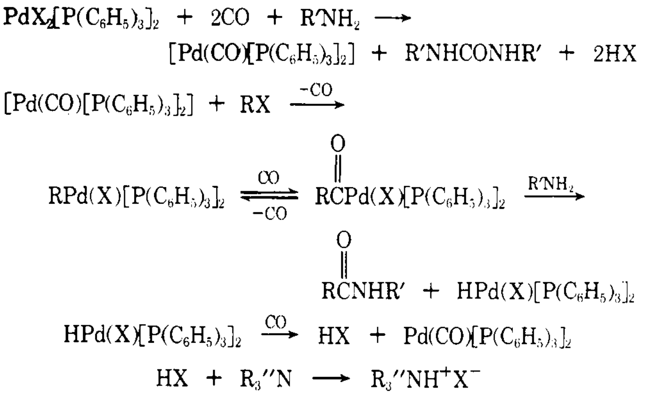
Halide	Amine (mm)	Catalyst	Temp, °C	Reaction time, hr ($T_{1/2}$, min)	Product (% yield)	Mp, °C	Molecular weight Found	Molecular weight Calcd
C_6H_5Br (108-86-1)	$C_6H_5NH_2$ (38)	$C_6H_5PdBr(PPh_3)_2$ (33381-14-5)	100	3.5 (41)	$C_6H_5CONHC_6H_5$ (94) (93-98-1)	162.5–163[b]	197.086	197.084
C_6H_5Br	$C_6H_5CH_2NH_2$ (25)	$PdBr_2(PPh_3)_2$ (23523-33-3)	100	3 (43)	$C_6H_5CONHCH_2C_6H_5$ (79) (1485-70-7)	105–105.5[c]	211.097	211.100
4-$CH_3OCOC_6H_4Br$ (619-42-1)	$C_6H_5NH_2$ (25)	$PdBr_2(PPh_3)_2$	100	3.5 (47)	4-$CH_3OCOC_6H_4CONHC_6H_5$ (86) (3814-10-6)	192–193[d]	255.090	255.090
4-$CH_3OC_6H_4Br$ (104-92-7)	$C_6H_5NH_2$ (25)	$PdBr_2(PPh_3)_2$	100	10 (85)	4-$CH_3OC_6H_4CONHC_6H_5$ (76) (7465-88-5)	173–174[e]	227.095	227.095
4-$NO_2C_6H_4Br$ (586-78-7)	$C_6H_5NH_2$ (25)	$PdBr_2(PPh_3)_2$	100	3.5 (80)[f]	4-$NO_2C_6H_4CONHC_6H_5$ (57) (619-80-7)	211–212[g]	242.065	242.069
4-$NO_2C_6H_4Br$	$C_6H_5NH_2$ (25)	$PdBr_2(PPh_3)_2$	100	7.5	4-$C_6H_5NHCONHC_6H_4CONHC_6H_5$ (33) (20643-51-8)	235–236	h	
				(−)[i]	4-$NO_2C_6H_4CONHC_6H_5$ (10)	211–212		
 (626-55-1)	$C_6H_5NH_2$ (25)	$PdBr_2(PPh_3)_2$	100	5.5 (75)	 (65) (1752-96-1)	118–119[j]	198.0649	198.0793
 (1003-09-4)	$C_6H_5NH_2$ (25)	$PdBr_2(PPh_3)_2$	100	2 (30)	 (63) (6846-13-5)	139–140[k]	203.0514	204.0399
 (588-72-7)	$C_6H_5NH_2$ (25)	$PdBr_2(PPh_3)_2$	60	3 (33)	 (81) (25775-89-7)	147–148[l]	223.097	223.100
	$C_4H_9N^{m,n}$ (50)	$PdBr_2(PPh_3)_2$	60	2.5 (29)	 (91) (52438-21-8)	100–100.5	201.112	201.115
 (588-73-8)	$C_6H_5NH_2$ (25)	$PdBr_2(PPh_3)_2$	60	4 (71)	 (80) (52393-67-6)	101–102	223.102	223.100
 (19647-26-8)	$C_6H_5NH_2$ (25)	$PdBr_2(PPh_3)_2$	100	1 (15)	 (87) (52393-68-7)	94–95[o]	237.1007	237.1154
 (16917-35-4)	$C_6H_5NH_2$ (25)	$PdBr_2(PPh_3)_2$	100	1 (20)	 (88) (21298-82-8)	119–119.5[p]	237.1178	237.1154

 (16403-09-1)	$C_6H_5NH_2$ (25)	$PdI_2(PPh_3)_2$ (23523-32-2)	100	1.5 (14)	 (52393-69-8)	(71)	96–97	203.128	203.130
 (16403-13-7)	$C_6H_5NH_2$ (25)	$PdI_2(PPh_3)_2$	100	1 (14)	 (52393-70-1)	(70)	66.5–67	203.127	203.130
 (557-98-2)	$C_6H_5NH_2$ (25)	$PdCl_2(PPh_3)_2$ (13965-03-2)	100	10	 (1611-83-2)	(74)	84–85[r]	161.0895	161.0841
 (40053-01-8)	$C_6H_5NH_2$ (25)	$PdBr_2(PPh_3)_2$	100	1.3 (30)	 (52393-83-2)	(80)	87–87.5[s]	219.0888	219.0895

[a] Carried out with 17.2 mm of halide, 19.0 mm of tri-n-butylamine, and 0.25 mm of catalyst under 1 atm of carbon monoxide. Registry numbers are given in parentheses. [b] Reported mp 160–161°, A. H. Blatt, Ed., "Organic Syntheses," Collect. Vol. I, Wiley, New York, N.Y., 1964, p 82. [c] Reported mp 105–106°, E. Beckman, *Ber.*, **37,** 4136 (1904). [d] Reported mp 193°, G. Renckhoff and H. L. Huekmann, U. S. Patent 3,252,977 (1966). [e] Reported mp 171°, A. Rossel, *Justus Liebigs Ann. Chem.*, **151,** 25 (1869). [f] Allowed to react until 17.4 mmol of CO had been absorbed. [g] Reported mp 212°, L. C. Raiford, R. Taft, and H. P. Lankelma, *J. Amer. Chem. Soc.*, **46,** 2051 (1924). [h] Parent ion not observed. Elemental analysis is reported in the Experimental Section. [i] Allowed to react until 27 mmol of CO had been absorbed. [j] Reported mp 124–126°, H. W. Grimmel, A. Guenther, and J. F. Morgan, *J. Amer. Chem. Soc.*, **68,** 539 (1946). [k] Reported mp 140°, "Thiophene and its Derivatives," Interscience, New York, N.Y., 1952, p 376. [l] Reported mp 151°, G. Tsatsas, *Bull. Soc. Chim, Fr.*, 1011 (1947). [m] Reaction carried out without tri-n-butylamine. [n] C_4H_9N is pyrrolidine. [o] Reported mp 95°, R. Stoermer, F. Grimm, and E. Lang, *Chem. Ber.*, **50,** 959 (1917). [p] Reported mp 121°, F. Henrich and A. Wirth, *Chem. Ber.*, **37,** 731 (1904). [q] Carried out with 100 mmol of organic halide, 30 mmol of tri-n-butylamine, and 0.50 mmol of catalyst at 135° under 600 psig of carbon monoxide. [r] Reported mp 87°, P. Bieber, *C. R. Acad. Sci.*, **231,** 291 (1950). [s] Reported mp 92°, R. Anschütz, *Justus Liebigs Ann. Chem.*, **353,** 139 (1907).

The mechanism of the amidation may involve an attack of the primary or secondary amine upon an acylpalladium intermediate. The reduction of the catalyst probably involves simultaneous formation of a substituted urea. Tris(triphenylphosphine)carbonylpalladium(0) and related carbonyls have been obtained under similar reaction conditions.[5] A possible reaction sequence is shown in Scheme I.

Scheme I



$$PdX_2[P(C_6H_5)_3]_2 + 2CO + R'NH_2 \longrightarrow [Pd(CO)[P(C_6H_5)_3]_2] + R'NHCONHR' + 2HX$$

$$[Pd(CO)[P(C_6H_5)_3]_2] + RX \xrightarrow{-CO}$$

$$RPd(X)[P(C_6H_5)_3]_2 \underset{-CO}{\overset{CO}{\rightleftharpoons}} R\overset{O}{\overset{\|}{C}}Pd(X)[P(C_6H_5)_3]_2 \xrightarrow{R'NH_2} R\overset{O}{\overset{\|}{C}}NHR' + HPd(X)[P(C_6H_5)_3]_2$$

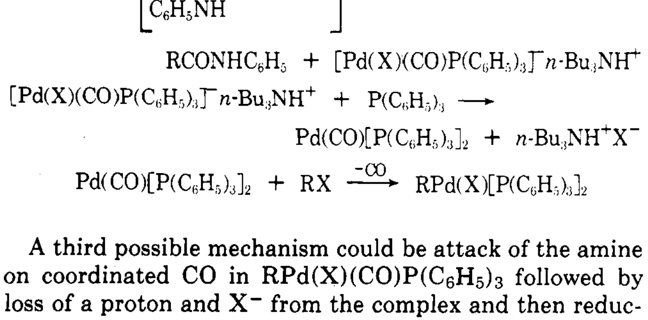
$$HPd(X)[P(C_6H_5)_3]_2 \xrightarrow{CO} HX + Pd(CO)[P(C_6H_5)_3]_2$$

$$HX + R_3''N \longrightarrow R_3''NH^+X^-$$

The fact that the reaction rates are faster with amines than with alcohols could mean that the rate determining step, at least in the amine reaction, is nucleophilic attack of the amine on an acylpalladium intermediate. The higher stereospecificity could mean that the alkenyl- and acylpalladium species are in equilibrium and that isomerization occurs slowly at the alkenyl stage. Since the amines react with the acyl complexes more rapidly than the alcohols do, there is less time for isomerization to occur. If this were the case, however, increasing the CO pressure probably would have increased the stereoselectivity of the carboalkoxylation, but it apparently did not in the one instance investigated. An alternative explanation could be that amine is coordinated to the palladium during the last stages of the reaction. The function of the tertiary amine in the aniline reaction or the strongly basic amine in other cases may be to remove a proton from the coordinated amine.

A mechanism such as shown in Scheme II could be imagined.

Scheme II



$$RPd(X)[P(C_6H_5)_3]_2 + CO \longrightarrow RCOPd(X)[P(C_6H_5)_3]_2 \overset{C_6H_5NH_2}{\rightleftharpoons} \underset{\displaystyle C_6H_5NH_2}{RCOPd(X)P(C_6H_5)_3} + P(C_6H_5)_3$$

$$\underset{\displaystyle C_6H_5NH_2}{RCOPd(X)P(C_6H_5)_3} + n\text{-}Bu_3N \rightleftharpoons \left[\underset{\displaystyle C_6H_5NH}{RCOPd(X)P(C_6H_5)_3}\right]^- n\text{-}Bu_3NH^+ \xrightarrow{CO}$$

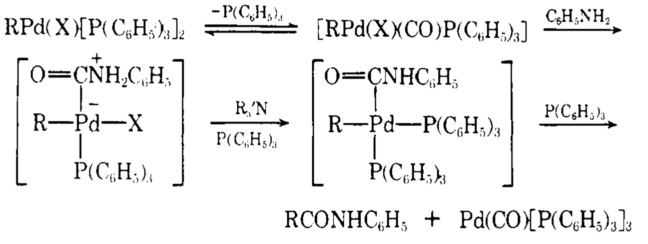
$$RCONHC_6H_5 + [Pd(X)(CO)P(C_6H_5)_3]^- n\text{-}Bu_3NH^+$$

$$[Pd(X)(CO)P(C_6H_5)_3]^- n\text{-}Bu_3NH^+ + P(C_6H_5)_3 \longrightarrow Pd(CO)[P(C_6H_5)_3]_2 + n\text{-}Bu_3NH^+X^-$$

$$Pd(CO)[P(C_6H_5)_3]_2 + RX \xrightarrow{-CO} RPd(X)[P(C_6H_5)_3]_2$$

A third possible mechanism could be attack of the amine on coordinated CO in $RPd(X)(CO)P(C_6H_5)_3$ followed by loss of a proton and X^- from the complex and then reductive elimination as shown in Scheme III.

Scheme III



The amidation reaction of aryl, heterocyclic, and vinylic halides is clearly a very convenient and useful method for producing a variety of substituted amides of aryl, heterocyclic, and α,β-unsaturated acids.

Experimental Section

General. The preparations and sources of the organic halides and catalysts used are given in the preceding paper[1] with one exception. *E*-Methyl 3-bromo-2-methylpropenoate was obtained as described by Canbere.[6] Molecular weights were determined by high resolution mass spectroscopy on a Du Pont (CEC) 21-170B double focus mass spectrometer. Proton nuclear magnetic resonance spectra were measured with a Varian Associates Model A-60A spectrometer or a Perkin-Elmer R-12B spectrometer in DMSO-d_6 or $CDCl_3$ using TMS as an internal standard.

Amidation Procedure. The general procedure used was similar to the one employed in the palladium-catalyzed carbobutoxylation of organic halides previously reported in detail.[1] Usually, 17.2 mmol of the organic halide, 25.0 mmol of the amine, and 19.0 mmol of tri-*n*-butylamine were allowed to react. If the amine being reacted was a strong base, tri-*n*-butylamine was not added and 50.0 mmol of the first amine was used. In the examples where a secondary anine was used, the product was not acid washed because secondary amides are acid soluble.

***N*-Phenylbenzamide.** The carbonylation apparatus containing catalyst suspended in a Teflon cup as described previously,[1] was flushed several times with carbon monoxide. A mixture of 2.7 g of bromobenzene (17.2 mmol) and 3.54 g of aniline (38.0 mmol) was added to the reaction vessel by means of a syringe. After equilibration of 100° (steam), the catalyst, $Pd(PPh_3)_2(Ph)(Br)$ (0.25 mmol), was added by dropping the Teflon cup into the stirred reaction mixture. Since after 1 hr only 12 ml of carbon monoxide had been absorbed, 3.6 g of tri-*n*-butylamine (19.0 mmol) was added and the up-take of carbon monoxide proceeded rapidly. Gas volume changes and times were periodically recorded. After 3.5 hr the absorption stopped (425 ml (17.4 mmol) of CO measured at 25° had been taken up). The reaction mixture was cooled, dissolved in ethyl ether (700 ml), and washed with several portions of 20% hydrochloric acid solution to remove salts and excess amine. The extracts were washed with several portions of distilled water. The ether layer was treated with decolorizing carbon, dried with anhydrous magnesium sulfate and filtered. The solid product formed after concentration of the solution was filtered and air-dried to give 2.89 g (94% yield) of *N*-phenylbenzamide, mp 162.5–163°.

***trans*-*N*-Cinnamoylpyrrolidine.** To the reaction vessel was added 3.12 g of *trans*-β-bromostyrene (17.2 mmol) and 3.56 g of pyrrolidine (50.0 mmol). After the reaction mixture was brought to equilibrium at 60° by means of a circulating constant temperature bath, under 1 atm of carbon monoxide, 0.198 g of $Pd(PPh_3)_2Br_2$ was added. Periodically, gas–volume changes and times were recorded until a total of 423 ml of CO had reacted. The reaction mixture was extracted with ether, and the extracts were washed with several portions of distilled water. The organic layer was concentrated *in vacuo* to remove the ether and excess pyrrolidine. The resulting solid obtained was dissolved in hot heptane, decolorized with charcoal, filtered, and cooled to give 3.15 g (91% yield) of *trans*-*N*-cinnamoylpyrrolidine, mp 100.0–100.5°.

Reaction of *cis*-β-Bromostyrene with CO and Pyrrolidine. *cis*-β-Bromostyrene, 17.2 mmol (92% cis, 8% trans) and pyrrolidine, 50.0 mmol, were treated as above in an attempt to make the *cis*-pyrrolidine amide of cinnamic acid. The CO uptake stopped after 200 ml (about half the theoretical amount) had reacted. The products were extracted with ether. The ether extracts were evaporated, and the oily residue was chromatographed on silica gel, first with pentane, followed by benzene, methylene chloride, and methanol. The pentane fraction was evaporated *in vacuo* to give 1.6 g (46%) of *cis*-1,4-diphenylbutenyne identified by its high resolution mass spectrum and nmr spectrum. Upon standing for several weeks at room temperature in the presence of light the oil crystallized to a solid (mp 93.5–95°) which by nmr was identified as *trans*-1,4-diphenylbutenyne. This cis to trans isomerization in the presence of light has been noted early.[4]

The trans isomer is reported to have a melting point of 96.5–97°. Evaporation of the methylene chloride eluate followed by crystallization from hot hexane gave 0.21 g (6.0%) of the *trans*-pyrrolidine amide of cinnamic acid. The methanol fraction gave 0.95 g of a viscous oil which could not be crystallized. This material contained a strong CO band at 1620 cm^{-1} and the nmr spectrum showed strong aromatic absorption with only weak vinyl absorptions.

N-Phenylamidation of *p*-Bromonitrobenzene. To the reaction vessel was added 3.47 g of *p*-nitrobromobenzene (17.2 mmol), 2.33 g of aniline (25.0 mmol), and 3.6 g of tri-*n*-butylamine (19.0 mmol). The reaction mixture was brought to equilibrium at 100°, with 1 atm of pressure of CO. The catalyst, $Pd(PPh_3)_2Br_2$ (0.25 mmol), was added and CO absorption began. The reaction was allowed to continue until a total of 660 ml of CO had been absorbed. The partially solid reaction mixture was extracted with ether, and the extracts were washed with 20% hydrochloric acid followed by saturated sodium bicarbonate, and then distilled water. The small amount of solid obtained which did not dissolve in the ether was dissolved in methylene chloride and the solution decolorized with charcoal, dried with anhydrous magnesium sulfate, and concentrated on a steam bath and cooled. The solid obtained (0.43 g, 10% of theory) had a melting point of 211–212° which is the same as the reported melting point for *N*-phenyl-*p*-nitrobenzamide.[7] This structure was confirmed by its high resolution mass spectrum and nmr spectrum. The ether soluble fraction was treated with charcoal, dried, filtered, and concentrated on a steam bath to about 100 ml. On cooling, 1.9 g of the *N*-phenylamide of 4-carboxydiphenylurea (33%) was obtained mp 233–235°. Recrystallization from ethanol raised the melting point to 235–236°.

Anal. Calcd for $C_{14}H_{10}O_2N_2$: C, 72.52; H, 5.13; N, 12.68. Found: C, 72.59; H, 5.42; N, 12.78.

Although the parent peak could not be observed in the high resolution mass spectrum, intense peaks were seen at *m/e* 93$^+$ and *m/e* 238$^+$ which indicate the expected decomposition products of the compound, aniline, and 4-*N*-phenylaminocarbonylphenylisocyanate, were being produced.

In order to improve the yield of *N*-phenyl-*p*-nitrobenzamide the above reaction was repeated but the reaction was stopped after 400 ml of CO had been absorbed. This procedure gave 3.44 g of crude amide that was recrystallized from acetone–hexane to give 2.32 g of pure *N*-phenyl-*p*-nitrobenzamide (57% yield).

***N*-Phenylmethacrylamide.** A mixture of 7.64 g (100 mmol) of 2-chloropropene, 2.33 g (25 mmol) of aniline, 5.56 g (30 mmol) of tri-*n*-butylamine, and 0.350 g (0.50 mmol) of $PdCl_2$ $(PPh_3)_2$ was placed in a 45-ml stainless steel high-pressure reactor with a magnetic stirring bar. The container was sealed, flushed with CO, pressured to 600 psig, and heated with stirring at 135° for 24 hr. The pressure dropped from 800 to 475 psi during this time. After cooling to room temperature the pressure was released and the reaction mixture was treated with 6 *N* hydrochloric acid and ether. The solids dissolved and the ether phase was separated, dried with anhydrous magnesium sulfate, filtered, and evaporated. The solid obtained was recrystallized from hexane to give 2.97 g of colorless crystals of product, mp 84–85°.

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Registry No.—Carbon monoxide, 630-08-0; aniline, 62-53-3; benzylamine, 100-46-9; pyrrolidine, 123-75-1; *cis*-1,4-diphenylbutenyne, 13343-78-7; *trans*-1,4-diphenylbutenyne, 13343-79-8.

Supplementary Material Available. Complete nmr spectra data for the compounds prepared will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche, referring to code number JOC-74-3327.

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Ceric Ammonium Nitrate Promoted Aromatic Substitution with Peroxydicarbonates[1]

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The decomposition of dialkyl peroxydicarbonates in the presence of a two-molar excess of ceric ammonium nitrate (CAN) in toluene led to tolyl alkyl carbonates in yields of 75–90% based on two carbonate moieties from each peroxide molecule. Unlike the previously reported catalytic effect of cupric chloride, where the chain-induced peroxide breakdown by cuprous limited the aryl ester yield to 1 mol/mol of peroxide, the CAN involvement was stoichiometric as both halves of the peroxide substituted onto the aromatic. No peroxide–cerous ion interaction seemed to occur; indeed the overall peroxide decomposition rate was actually retarded relative to that in the absence of metal salts and all the cerium was recovered as cerous nitrate. Based on isomer distributions and relative rates the substituting entity possessed more selectivity than the free carbonate radicals. No polymer production was noted in reactions performed with acrylonitrile, suggesting low oxy radical concentrations. The importance of the hexanitrato cerium(IV) complex as an oxidant in the overall aromatic substitution process was established by studying a variety of other ceric and cerous salts in this reaction.

The decomposition of peroxydicarbonates and diacyl peroxides in the presence of toluene can be modified by the inclusion of suitable redox agents (*e.g.*, $CuCl_2$,[2] $FeCl_3$,[3] I_2,[4] O_2,[5] and various other metal salts[3,6]) which oxidize oxy radical–aromatic adducts to form aryl esters. With most of the metal salts a lower valence inorganic species is produced which then reduces the peroxide, leading to a chain reaction.[2,3] The net stoichiometry is indicated in eq 1 for cupric chloride, which proved to be the most effective metal salt,

$$(RCO_2)_2 + ArH \xrightarrow[CH_3CN]{CuCl_2} RCO_2Ar + RCO_2H \qquad (1)$$

$$R = i\text{-PrO or } C_6H_5$$

forming nearly 1 mol of aryl ester/mol of peroxide.[2] With molecular oxygen as a promoter the reaction went by a nonchain mechanism and aryl ester yields somewhat in excess of 1 mol/mol of peroxide were realized.[5] In the absence of added oxidant less than 1% nuclear oxygenation resulted, as the oxy radicals reacted by other pathways.

Recently we found that use of sufficient quantities of ceric ammonium nitrate (CAN) with the same peroxides and toluene led to nearly doubled aromatic oxygenation yields, and we wish to report on the details of this reaction.

Results and Discussion

Reaction Products. The optimum general procedure involved adding a solution of known concentration of diisopropyl peroxydicarbonate (IPP) in toluene to a 2.25 molar excess of CAN, and a 25- to 50-fold molar excess of toluene in acetonitrile at 60°, and allowing the reaction to go for 24 hr. Table I summarizes the organic reaction products.

Apparently, both oxy fragments formed from peroxide homolysis were capable of reacting with the aromatic, as 1.6 mol of oxygenation products (tolyl isopropyl carbonates) were formed from 1 mol of peroxide. This meant that 80% of the potential alkoxycarboxy moieties (2 mol/mol of peroxide) added to the ring, while the remaining 20% decomposed to form carbon dioxide, acetone, and isopropyl alcohol. The material balance based on starting peroxide was excellent in all cases.

Table I
Organic Reaction Products from Diisopropyl Peroxydicarbonate–Toluene–Ceric Ammonium Nitrate System[a]

Product	Yield,[b] %
Tolyl isopropyl carbonates[c]	160
Isopropyl alcohol	26
Acetone	16
Carbon dioxide	47
Benzaldehyde	4
Benzyl alcohol	2
Nitrotoluenes	1
$\sum(CO_2)^d$	103
$\sum(i\text{-Pr})^e$	101

[a] Toluene:CAN:peroxide = 25:2.25:1, acetonitrile solvent, 60°, 24 hr (see general procedure). [b] Based on 1 mol of product/mol of peroxide. [c] Isomer distribution, ortho:meta:para = 56.2:11.8:32.0. [d] Material balance based on two CO_2 groups/mol of peroxide. [e] Material balance based on two isopropyl groups/mol of peroxide.

As the reaction proceeded, crystals of cerous nitrate gradually precipitated from the reaction mixture. This and all the other inorganic reaction products were isolated and quantitatively determined (Table II) utilizing total acid, ammonium ion, nitrate ion, and cerium analyses. On the basis of these product studies (Tables I and II), the following stoichiometry was proposed for the reaction (eq 2).

$$(i\text{-PrOCO}_2)_2 + 2(NH_4)_2Ce(NO_3)_6 + 2C_6H_5CH_3 \longrightarrow 2i\text{-PrOCO}_2C_6H_4CH_3 + 2Ce(NO_3)_3 + 4NH_4NO_3 + 2HNO_3 \qquad (2)$$

Normally, cerous nitrate is soluble in acetonitrile, but apparently it is salted out by ammonium nitrate and nitric