mg-atom) of lithium pieces in 20 mL of THF at −65 °C. After 3 h, samples of the mixture were withdrawn and examined at 0 °C by ^{1}H NMR spectroscopy. In the regions free of THF absorptions (2.0–3.2 and 3.9–8.0 ppm), the development of new signals was monitored at intervals of 15 s. Signals attributable to the reaction products were observed, but neither enhanced nor emission signals could be detected. After 5 h, the usual hydrolytic workup again led to the isolation of 1,1,1-triphenylethane and 1,1,2-triphenylethane.

Bis(2,2,2-triphenylethyl)mercury (24) with *n*-Butyllithium. (a) Labeling of the (2,2,2-Triphenylethyl)lithium Intermediate (25). Under nitrogen, a solution of 500 mg (0.69 mmol) of **24** in 30 mL of THF was treated below −65 °C with 2.5 mL of 1.6 M *n*-butyllithium in hexane. After 2 h at this temperature, the reaction mixture was treated with 2 mL of deuterium oxide (99.8%). Usual workup (cf. supra) gave 300 mg of oil, which was crystallized from ethanol to yield 200 mg of colorless 1,1,1-triphenylethane (**21**), mp 92–94 °C, which did not depress the melting point of an authentic sample. That this **21** was monodeuteriated on the methyl group was established by spectral measurements: MS, *m/e* (relative intensity) (at 70 eV) 259 (74), 243 (100), 185 (51), 165 (70), 77 (32); ^{1}H NMR ($CDCl_3$) δ 2.2 (s, 2 H, CH_2), 6.9–7.4 (m, 15 H).

(b) ESR Monitoring of the Rearrangement. A solution of 50 mg of **24** and 0.5 mL of THF in an ESR tube equipped with a rubber septum was treated under nitrogen at −60 °C with 0.5 mL of 1.6 M *n*-butyllithium. After 30 min at −60 °C, the tube was placed in an ESR spectrometer probe maintained at −60 °C. Thereafter, spectral scans were taken at ranges of 1000 and 250 G for the following elapsed times and temperatures: 0.5 h, −60 °C; 1 h, 0 °C and 20 °C; and 2.5 h, 0 °C. No ESR signal could be detected in any of the spectral runs. After a total of 4 h with a maximum temperature of 0 °C, the reaction mixture was hydrolyzed and worked up. Spectral analysis indicated the presence of a mixture of 1,1,1- and 1,1,2-triphenylethanes.

(c) ^{1}H NMR Monitoring of the Rearrangement. A similar reaction between 119 mg of **24** in 0.5 mL of tetrahydrofuran-d_8 and 0.3 mL of 1.6 N *n*-butyllithium at −65 °C was observed by ^{1}H NMR spectroscopy at 40 °C. The two singlets at 2.05 and 7.12 ppm, which arise from **24**, quickly disappeared, and a new singlet grew in at 3.9 ppm. No emission signal could be observed. The aromatic proton region simultaneously changed from a singlet to three broad peaks, roughly split into triplets, at 5.8, 6.6, and 7.1 ppm. Usual hydrolytic workup showed that 1,1,2-triphenylethane was the major product.

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Registry No. **11**, 118716-46-4; **11** (lithium salt), 118716-54-4; **12**, 118716-47-5; **12** (lithium salt), 118716-55-5; **13**, 161-25-1; **13** (lithium salt), 118716-56-6; **14**, 30319-92-7; **15**, 13355-64-1; **15** (lithium salt), 118716-57-7; **16**, 92-83-1; **17**, 118716-48-6; **18**, 61076-90-2; **19**, 35377-96-9; **21**, 5271-39-6; **22**, 111584-33-9; **23**, 33885-01-7; **24**, 118716-50-0; **25**, 16536-63-3; **26** (R = R′ = Ph), 118716-43-1; **26** (R = CH_3, R′ = Ph), 118716-45-3; **27**, 118716-44-2; **28**, 13355-65-2; **31** (R, Ar = Ph), 602-15-3; **31** (R = Me, Ar = Ph), 33498-62-3; **33**, 2720-93-6; **34**, 31859-87-7; **36**, 4425-68-7; **39**, 118716-52-2; Ph_3CCH_2D, 118716-49-7; 2-(bromomethyl)biphenyl, 19853-09-9; benzophenone, 119-61-9; acetophenone, 98-86-2; 9-fluorenone, 486-25-9; 1,2-bis(2-biphenylyl)ethane, 96003-60-0; 9-methylfluorene, 2523-37-7; 9-phenylfluorene, 789-24-2; triphenylmethane, 519-73-3; 1,2,2,3,3,4-hexaphenylbutane, 118716-51-1; *trans*-9,10-diphenyl-9,10-dihydrophenanthrene, 25127-93-9; *trans*-9-deuterio-9,10-diphenyl-9,10-dihydrophenanthrene, 118722-50-2; dihydrodibenzo[*g,p*]chrysene, 5162-39-0; 1,2,2-triphenylhexane, 118716-53-3; 3,3,3-triphenylpropionic acid, 900-91-4.

Applications of Ammonium Formate Catalytic Transfer Hydrogenation. 6.[1] Analysis of Catalyst, Donor Quantity, and Solvent Effects upon the Efficacy of Dechlorination

Mohmed K. Anwer, Douglas B. Sherman, J. Gordon Roney, and Arno F. Spatola*

Department of Chemistry, University of Louisville, Louisville, Kentucky 40292

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Dehalogenation reactions have important synthetic and environmental potential and can be achieved by a variety of chemical methods, including transfer hydrogenation. A catalytic transfer hydrogenation procedure utilizing ammonium formate as an in situ hydrogen donor has previously been used for the dechlorination of polychlorinated biphenyls and for the deuterium labeling of chlorinated peptides. In this study, a systematic evaluation of the effects of catalyst, donor quantity, temperature, and solvent on ammonium formate catalytic transfer hydrogenolyses of aryl chlorides has been undertaken. Results indicate that carbon was the most effective support among those surveyed, and a 3% palladium loading and 2 equiv of ammonium formate were adequate in terms of overall reaction rate and cost. Catalysts with low Pd content were found to benefit from an increase in temperature, as did reactions involving highly hydrophobic substrates. Alcohols proved to be more effective than polar aprotic (HMPA) and nonpolar (THF, dioxane) solvents. Thus, 1-chloronaphthalene was quantitatively dechlorinated in C_2 and C_3 alcohols in 2 h and in 4 h in HMPA. The reaction was only 51% complete in THF and 30% complete in 1,4-dioxane after 4 h. Improved reaction procedures emerging from these studies were then used for the dechlorination of a variety of mono- and polychlorinated aromatic compounds.

Hydrogenation is a convenient method for the dehalogenation of aryl halides because of its experimental simplicity, good yields, and high purity of products.[2] However, the low solubility of hydrogen gas in organic solvents presents a limitation that is best overcome by the employment of high-pressure reactors. This difficulty may also be circumvented through catalytic transfer hydrogenation (CTH), in which simple organic/inorganic molecules, such as cyclohexene,[3] cyclohexadiene,[4] formic acid,[5]

(1) Part 5. Anwer, M. K.; Porter, R. A.; Spatola, A. F. *Int. J. Peptide Protein Res.* **1987**, *30*, 489.
(2) Pinder, A. R. *Synthesis* **1980**, 425.
(3) (a) Braude, E. A.; Linstead, R. P. *J. Chem. Soc.* **1954**, 3544. (b) Brieger, G.; Nestrick, T. J. *Chem. Rev.* **1974**, *74*, 567. (c) Viswanatha, V.; Hruby, V. J. *J. Org. Chem.* **1980**, *45*, 2010.
(4) Felix, A. M.; Heimer, E. P.; Lambros, T. J.; Tzougraki, C.; Meienhofer, J. *J. Org. Chem.* **1978**, *43*, 4194.

0022-3263/89/1954-1284$01.50/0

hydrazine,[6] and phosphinic acid[7] act as in situ sources of hydrogen. Consequently, CTH reactions may be performed at atmospheric pressure and proceed without the additional restricting phase boundaries between hydrogen gas and solvent and/or catalyst in the conventional technique.

We first reported on the utility of ammonium formate as an in situ hydrogen donor for the heterogeneous catalytic transfer hydrogenolysis of protecting groups commonly employed in peptide chemistry, such as the *N*-benzyloxycarbonyl, N^g-nitro, benzyl ester, and benzyl ether functionalities.[8] The ease and rapidity of this reductive hydrogenolytic methodology was further apparent in our reports detailing its application to the cleavage of the benzyl ester linkage employed as an anchor in Merrifield solid phase peptide synthesis,[9,10] as well as in the dechlorination of aryl chlorides, including such environmental contaminants as polychlorinated biphenyls (PCB's)/phenols.[11] Its reductive potential in the hydrogenation of unsaturated C=C bonds and in conversion of aromatic nitro groups to arylamines has also been demonstrated, as has its sensitivity to the presence of divalent sulfur and inertness to tetra- and hexavalent sulfur.[12] The wide applicability of the ammonium formate catalytic transfer hydrogenation (AF-CTH) process has been further documented by others in such diverse transformations as in the conversion of arylcyano to arylmethyl groups,[13] azides to amines,[14] debenzylation of *O*-[8,15] and *N*-benzyl[16] derivatives, the rapid synthesis of α-amino acids from α-nitro acid/esters,[17] and in *N*-dephenylethylation.[18]

In most of the studies cited above, the catalyst of choice has been either 10% Pd/C or 20% $Pd(OH)_2/C$ along with a large excess of ammonium formate as the hydrogen donor. However, there have been no attempts to systematically evaluate the various components of the AF-CTH process. In view of this, and since hydrogenolysis of PCB's is known to be free of byproducts such as halogenated dioxins/dibenzofurans that accompany their pyrolytic destruction, it has been our continuing interest to explore further the scope of AF-CTH in partial relevance to this problem. Our efforts to understand the effects of catalyst, temperature, solvent, and donor quantity variations on the extent of dechlorination in model systems are the subject of this study.

Table I. Effect of Varying Catalyst Support on Ammonium Formate Catalytic Transfer Hydrogenolysis of 4-Chloroanisole at Room Temperature[a]

catalyst	reaction time,[b] min	% anisole formed
5% Pd/C	20	100
5% Pd/Al_2O_3	120[c]	1.7
5% Pd/Kieselguhr	30[c]	<0.1
5% $Pd/BaSO_4$	30[c]	<0.2
5% $Pd/CaCO_3$	30[c,d]	0
10% Pd/C	30	99
10% Pd/Al_2O_3	30[c]	6.9

[a] Reaction conditions: See the Experimental Section. HPLC parameters were the same as system II in Table IV, except the flow was 1.0 mL/min. [b] Aliquots were removed at 20, 30, 60, 120, 180, and 240 min and assayed by RP-HPLC. [c] No improvement in product yield was observed with increased reaction times. [d] Catalyst was only feebly active even after treatment with NH_4^+-$HCOO^-$ for 24 h.

Results and Discussion

It has been reported that the order of reductive dehalogenation is benzylic and allylic halides > aryl, vinyl, acyl halides ≫ aliphatic halides. Within the same structural environment, the ease of hydrogenolysis of the organic–halogen bond is I > Br > Cl ≫ F.[19] Yet, the hydrogenolyses of organic iodides/bromides are often rendered difficult by the liberated HI/HBr (soft bases according to Pearson's hard–soft acid–base theory), which interact strongly with Pd metal, the soft acid.[19b,20] Addition of a base such as Na_2CO_3, NaOAc, or NaOH is known to benefit the progress of these reactions by converting the HI/HBr initially formed to the comparatively harder bases I^-/Br^-, which now have a relatively lowered affinity for the Pd metal.[19b] For organic chlorides, the contribution of such an interaction may not be as pronounced during hydrogenolysis. In the AF-CTH technique, the donor disproportionation product, ammonia, appears to adequately adopt the role of HCl scavenger. Thus, the AF-CTH dechlorination of a standard Aroclor 1254 sample was achieved in 4 min, and no external base had been added.[11]

Our preliminary experiments with bromides suggested that debromination benefits from the addition of an external base but was still consistently slower than dechlorination. Furthermore, in an interesting competition experiment using 1-chloro-4-bromobenzene (unpublished results), the bromine was actually removed preferentially, although again the reaction rate was slower. We and others[17a] have noted that the problem of dehalogenating aryl bromides and iodides is considerably more complex than for aryl chlorides, and we have thus decided to restrict this study to the chlorides.

In a typical experiment, the quantity of substrate was chosen to contain 10 mmol of chlorine bound to the aromatic nuclei, and the substrate was dissolved in a suitable solvent. Prior to the addition of solvent to Pd/C catalysts, it was essential either to wet the catalysts with water or to maintain an inert atmosphere (e.g., a blanket of CO_2) to overcome the hazard of fire that usually accompanies the addition of a combustible organic solvent to a catalyst exposed to air or oxygen. To initiate the reaction, 20 mmol of ammonium formate in H_2O was added to the suspended catalyst followed by the solution of the substrate. An

(5) ElAmin, B.; Anantharamaiah, G. M.; Royer, G. P.; Means, G. E. *J. Org. Chem.* **1979**, *44*, 3442.
(6) (a) Furst, A.; Berlo, R. C.; Hooton, S. *Chem. Rev.* **1965**, *65*, 51. (b) Anwer, M. K.; Khan, S. A.; Sivanandaiah, K. M. *Synthesis* **1978**, 751.
(7) (a) Entwistle, I. D.; Johnstone, R. A. W.; Telford, R. P. *J. Chem. Res. (S)* **1977**, 117. (b) Entwistle, I. D.; Gilkerson, T.; Johnstone, R. A. W.; Telford, R. P. *Tetrahedron* **1978**, *34*, 213.
(8) Anwer, M. K.; Spatola, A. F. *Synthesis* **1980**, 929.
(9) Anwer, M. K.; Spatola, A. F. *Tetrahedron Lett.* **1981**, 4369.
(10) Anwer, M. K.; Spatola, A. F.; Bossinger, C. D.; Flanigan, E.; Liu, R. C.; Olsen, D. B.; Stevenson, D. *J. Org. Chem.* **1983**, *48*, 3503.
(11) Anwer, M. K.; Spatola, A. F. *Tetrahedron Lett.* **1985**, 1381.
(12) (a) Anwer, M. K. Ph.D. Thesis, University of Louisville, January, 1985. (b) Altman, J.; Shoef, N.; Wilchek, M.; Warshawsky, A. *J. Chem. Soc., Chem. Commun.* **1985**, 1133. (c) Meldal, M. *Acta Chem. Scand.* **1986**, *B40*, 242. (d) Meldal, M. *Acta Chem. Scand.* **1986**, *B40*, 250. (e) Evin, G.; Devin, J.; Menard, J.; Corvol, P.; Castro, B. In *Proceedings of the 8th American Peptide Symposium*; Hruby, V. J., Rich, D H., Eds.; Pierce Chemical Co.: Rockford, IL, 1983; p 591.
(13) Brown, G. R.; Foubister, A. J. *Synthesis* **1982**, 1036.
(14) Gartiser, T.; Selve, C.; Delpuech, J.-J. *Tetrahedron Lett.* **1983**, 1609.
(15) Bieg, T.; Szeja, W. *Synthesis* **1985**, 76.
(16) (a) Overman, L. E.; Sugai, S. *Helv. Chim. Acta* **1985**, *68*, 745. (b) Adger, B. M.; O'Farrell, C.; Lewis, N. J.; Mitchell, M. B. *Synthesis* **1987**, 53.
(17) (a) Ram, S.; Ehrenkaufer, R. E. *Tetrahedron Lett.* **1984**, 3415. (b) Ram, S.; Ehrenkaufer, R. E. *Synthesis* **1986**, 133.
(18) Carpino, L.; Tunga, A. *J. Org. Chem.* **1986**, *51*, 1930.
(19) (a) Rylander, P. N. In *Catalytic Hydrogenation in Organic Synthesis*; Academic Press: New York, 1979. (b) Kiebom, A. P. G.; Van Rantwijk, R. In *Hydrogenation and Hydrogenolysis in Synthetic Organic Chemistry*; Delft University Press: Delft, The Netherlands, 1977.
(20) Pearson, R. G.; Songstad, J. *J. Am. Chem. Soc.* **1967**, *89*, 1827.

Table II. Effect of Temperature on the AF-CTH Dehalogenation[a]

substrate	catalyst[b]	reaction time, min (temp)	solvent	product	% yield[c]
2-chlorotoluene	1% Pd/C	90 (RT)	MeOH	toluene	90
2-chlorotoluene	1% Pd/C	10 (reflux)	MeOH	toluene	100
4-chlorotoluene	1% Pd/C	90 (RT)	MeOH	toluene	80
4-chlorotoluene	1% Pd/C	15 (reflux)	MeOH	toluene	95
4-chlorotoluene	3% Pd/C	15 (RT)	EtOH	toluene	100
4-chlorotoluene	3% Pd/C	15 (reflux)	EtOH	toluene	100
1-chloronaphthalene[d]	3% Pd/C	120 (RT)	2-propanol	naphthalene	100
1-chloronaphthalene[d]	3% Pd/C	30 (reflux)	2-propanol	naphthalene	100
2-chlorobenzoic acid	1% Pd/C[e]	60 (RT)	EtOH	benzoic acid	17
2-chlorobenzoic acid	1% Pd/C[e,f]	60 (reflux)	EtOH	benzoic acid	88

[a] HPLC parameters may be found in Table V. 2-Chlorobenzoic acid was assayed by system IV. [b] 0.5 g of catalyst was used for 10 mm of substrate in alcohol (20 mL). A large excess of ammonium formate was used in each case. [c] Yields were calculated from normalized areas for standard samples of substrate and product. [d] Data from Tables IV and V. [e] 1.5 g of 1% Pd/C granules used instead. [f] When the granules were ground to a powder and the reaction was repeated, there was no significant change in the results.

additional portion of the same donor quantity was added 30 min after the reaction had begun. Aliquots were removed at suitable intervals of time and were assayed by reversed-phase high-performance liquid chromatography (RP-HPLC). The progress of the reaction was quantitated from the UV extinction coefficients of the substrate(s) and product(s).

It was observed at ambient conditions that the order of addition of reagents had a significant effect on catalysts with low Pd loadings or when the substrate adsorbed strongly to the catalyst. For example, complete dechlorination of 4-chlorotoluene occurred in <15 min at room temperature when ammonium formate was added to the catalyst (5% Pd/C) prior to the introduction of the substrate, while the same reaction took about 90 min when the donor was added after the substrate. At higher temperatures, the sequence of addition appeared to have little effect, if any, on the reaction rate. Since most of the AF-CTH reactions were performed at ambient temperature and pressure, the addition of ammonium formate either in the solid form or as an aqueous solution should precede that of the substrate.

The Role of Catalyst Support. In order to examine the effects of catalyst support on the AF-CTH process, 4-chloroanisole was reacted with either a 5 or a 10% Pd loading on carbon, Al_2O_3, kieselguhr, $BaSO_4$, or $CaCO_3$. As shown in Table I, carbon significantly outperformed the other supports. For example, dechlorination under ambient conditions was complete in 20 min with 5% Pd/C, whereas the reaction with 5% Pd/Al_2O_3 was only 1.7% complete after 120 min. It should be noted that, except for $CaCO_3$, evolution of gases was observed during both activation with ammonium formate and during the reaction itself.

$CaCO_3$ or $BaSO_4$ supports for Pd are usually employed to achieve a downward modulation of their catalytic activity so as to attain selective reductions.[19] In fact, a diminished rate of gas evolution may be noted when using either $CaCO_3$ or $BaSO_4$ supports, compared to Pd/C, even in the absence of added substrate. We have previously shown[8] that 10% palladium on carbon is a suitable catalyst when used for benzyl group deprotection by ammonium formate even though the same reaction required the more expensive palladium black when using formic acid as donor. In any case, carbon, possibly due to its similar hydrophobic nature with respect to the substrate, may assist in the adsorption of substrate to the catalyst and, as a consequence, result in substantial gains in reaction rates.

Effect of Temperature. An attractive feature of most AF-CTH processes is that they proceed rapidly at room temperature and pressure. For example, we have shown that nitroarginine can be deprotected in 5–10 min,[8] and it has also been demonstrated that several α-nitro esters could be reduced to the corresponding α-amino esters within 10 min with 10% Pd/C in methanol.[17a] Variations in temperature can affect a number of reaction parameters, including adsorption and desorption processes of donor, substrate, and product, as well as influencing reaction rates and solubility of products. For example, when strong hydrophobic interactions between the substrate and support prevail, an increase in temperature can have a beneficial effect on the reaction rate. Thus, while decarbobenzoxylation of Cbz-Ile-O^{t}Bu with 10% Pd/C was complete in 10 min, the reaction for the more hydrophobic peptide Cbz-D-Val-Leu-Ile-O^{t}Bu was incomplete even after 4 h at room temperature.[21] In addition, considerable agglomeration of the catalyst had occurred. For the latter reaction, it was necessary to use refluxing conditions to drive the reaction to completion.

An increase in temperature also appears to have a beneficial effect when the catalyst has a lower Pd loading. This is illustrated in Table II, in which several substrates were dechlorinated with 1% or 3% Pd/C. While 100% naphthalene formed from 1-chloronaphthalene in 120 min under ambient conditions with 3% Pd/C, the reaction was quantitative in 30 min at reflux. A similar effect was observed for 2-chlorotoluene and 1% Pd/C in methanol. Here the reaction was 90% complete after 90 min at room temperature and quantitative in 10 min at reflux.

It should also be noted that the dechlorination of 2-chlorotoluene could be effected in 30 min under ambient conditions when 3% Pd/C and 2-propanol were employed (Table V). On the whole, these results suggest that increasing either the reaction temperature or the Pd content can have a similar beneficial effect. However, when agglomeration of substrate and catalyst occurs, then increasing the reaction temperature appears to be the better choice.

Variation of the Amount of Transfer Reagent with Respect to Metal Loading. We have shown earlier that on an equal metal content basis, 10% Pd/C performed better than 1% Pd/C in the AF-CTH reaction of 2,4,6-trichlorophenol.[12a] Thus, under similar reaction conditions, 97.8% phenol and 2.2% 2-chlorophenol formed after 16 h with 10% Pd/C. In contrast, with 1% Pd/C, 34.6% phenol, 12.1% 2-chlorophenol, 4.2% 2,6-dichlorophenol, and 20.1% 2,4-dichlorophenol formed. In the latter case, 29.1% of 2,4,6-trichlorophenol was left unreacted. This suggested that the proximity of Pd atoms in a supported catalyst may have a bearing on the extent of dechlorination (assuming a *relatively* uniform distribution of metal). Furthermore, selectivity was not attained because phenol had formed even during the early stages of reaction. The

(21) Sherman, D. B.; Anwer, M. K.; Spatola, A. F. Unpublished results.

Table III. Effect of Solvent on AF-CTH of 2-Chlorobenzoic Acid[a,b]

solvent	% benzoic acid formed with time, min								
	5	10	20	30	45	60	120	180	240
methanol	9.0/20.9	12.6/27.5	16.1/39.9	19.5/48.4	nd[c]/58.8	29.7/100	47.6/-	54.4/-	60.0/-
ethanol	29.1/34.3	42.8/52.4	63.6/72.0	79.0/100					
1-propanol	35.6/29.7	48.6/46.2	76.7/68.8	82.5/81.5	100/100				
2-propanol	46.6/35.6	63.7/52.8	86.1/74.5	94.7/86.7	100/100				
tert-butyl alcohol	36.1/27.8	53.4/46.2	75.1/67.3	99.9/79.6	100/100				
HMPA	9.9/10.1	15.4/15.9	24.9/23.2	31.5/30.8	37.4/38.9	45.5/44.9	nd	nd/75.7	nd/83.7
tetrahydrofuran	26.0/25.4	57.1/43.4	81.5/70.3	100/88.9	-/100				
1,4-dioxane	10.9/4.0	21.1/14.6	36.9/29.4	46.2/40.0	59.9/55.6	71.1/67.6	nd	100/100	
ethyl acetate	17.9/12.6	55.7/39.8	76.8/71.0	85.3/83.5	nd/100	100/-			

[a] HPLC parameters employed those of system IV in Table V. [b] The first entry in each column represents the amount of benzoic acid formed when the substrate was added 1 min after the addition of aqueous ammonium formate. The second entry represents the amount of benzoic acid formed when the catalyst was presaturated by stirring with solid ammonium formate for 10–30 min prior to the introduction of substrate and additional aqueous ammonium formate. [c] Not determined.

Table IV. Effect of Solvent on AF-CTH of 1-Chloronaphthalene[a] (Presaturation)

solvent	% naphthalene formed with time, min								
	5	10	20	30	45	60	120	180	240
methanol	7.3	10.2	14.1	17.1	21.3	24.7	34.4		
ethanol	24.3	36.2	56.5	71.7	87.4	98.5	100		
1-propanol	17.1	25.3	38.1	49.2	62.8	73.4	99.4		
2-propanol	12.6	19.1	66.0	66.0	87.5	99.2	100		
tert-butyl alcohol	20.4	29.7	61.1	61.1	76.6	91.7	99.9		
HMPA	8.4	21.4	47.3	47.3	62.5	74.9	98.6	99.9	100
80% aqueous AcOH	5.4	5.98	5.2	5.2	4.9	5.0	4.9	4.8	5.0
tetrahydrofuran	5.1	12.0	29.0	29.0	36.8	42.2	51.2	51.3	51.6
1,4-dioxane	0.3	0.2	3.5	3.5	6.1	8.6	17.1	24.0	29.5[b]
ethyl acetate	3.4	5.6	18.6	18.6	28.6	36.3	58.78	62.6	79.9[c]

[a] HPLC parameters may be found in Table V. [b] 99.76% at 24 h. [c] 99.97% at 24 h.

differences in the amounts of various phenols formed may be indicative of the difference in the efficiency of hydrogen transfer of the two catalysts. Therefore, we chose to examine the relationship of the quantity of donor needed to effect complete dechlorination with a given Pd loading.

Our selection of 2-chlorobenzoic acid was based on the simplicity of the reaction course, i.e., a monochloro compound versus a trichlorophenol. Accordingly, a series of individual experiments with varying amounts of ammonium formate (0.2, 0.5, 0.7, 1.0, and 2.0 mmol) were performed with a constant quantity of 2-chlorobenzoic acid (1.0 mmol) in methanol (5 mL) and 10% Pd/C (50 mg) under refluxing conditions. After 20 min, an aliquot was removed and assayed by RP-HPLC. Similar experiments were also performed for each of the supported Pd catalysts shown in Figure 1. Complete dechlorination was observed for 3%, 5%, and 10% Pd/C when a 2-fold excess of ammonium formate was used. In contrast, only 24% benzoic acid formed with 1% Pd/C.

Among the catalysts that were studied, it was seen that the efficacy of hydrogen transfer or product formation increased with increasing Pd loading. Catalysts with relatively poor efficiency in hydrogen transfer, such as 1% Pd/C, or substrates that react sluggishly may benefit from a periodic addition of ammonium formate, since its disproportionation is observed even in the absence of substrate. In consideration of these observations, 3% Pd/C appears to be an economical and efficient choice of catalyst.

Effect of Solvent. Generally, solvents such as MeOH, EtOH, EtOAc, or AcOH are used in dehalogenation reactions, but most AF-CTH reactions reported to date have employed MeOH. It is well known that alcohols can function as good hydrogen donors,[22] and it has been proposed that the nature of hydrogen displacing the aryl-bound halogen may be hydridic.[23] However, solubility considerations may sometimes warrant the use of nonpolar solvents. For example, Aroclor 1254 is sparingly soluble in MeOH but will remain in solution if first dissolved in THF. If the solvent is too nonpolar, agglomeration of catalyst can occur. To evaluate such interactions between the solvent and the catalyst/support, representative polar (protic and aprotic) and nonpolar solvents were chosen, and their effect on the dechlorination of two model compounds, 2-chlorobenzoic acid (Table III) and 1-chloronaphthalene (Table IV), was studied.

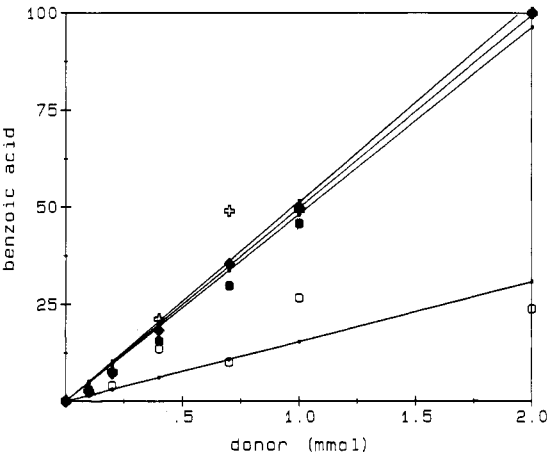

Figure 1. Least-squares plot of the relationship between the extent of dechlorination of 2-chlorobenzoic acid and quantity of donor (ammonium formate) after 20 min at reflux. Catalysts used were the following: □, 1% Pd/C; ■, 3% Pd/C; ◆, 5% Pd/C; ✣, 10% Pd/C. Note that only 24% benzoic acid formed with 1% Pd/C even with excess donor.

(22) (a) Kleiderer, E. C.; Kornfeld, E. C. *J. Org. Chem.* **1948**, *13*, 455. (b) Andrews, M. J.; Pillai, C. N. *Indian J. Chem. Sect. B* **1978**, *16*, 465.

(23) Kraus, M.; Bazant, V. In *Catalysis*; Hightower, J. W., Ed.; American Elsevier: New York, 1973; Vol. 2, p 1073.

The experiments with 2-chlorobenozic acid were performed by two different methods. In the first method, an aqueous solution of ammonium formate was added to the catalyst and solvent and then stirred for 1 min. Following this short activation time, the substrate was added to the mixture. The amounts of benzoic acid formed at selected time intervals are reported as the first entry in each column of Table III.

In the second method, solid ammonium formate was added to catalyst and solvent, and the mixture was stirred for 10–30 min. Afterward, the substrate and aqueous ammonium formate were added. This "presaturation" procedure appeared to have a beneficial effect on the rate of several dechlorination reactions in methanol, and we were curious as to whether this pretreatment advantage would carry over to other solvents. The amounts of benzoic acid thus formed are reported as the second entry in each column of Table III.

For the reactions carried out with a 1-min activation period, the amount of time required for completion of reaction varies from 45 to >240 min. Most surprisingly, the reaction with MeOH was only 60% complete after 240 min. Reactions involving other alcohols, such as 1-propanol and 2-propanol, proceeded more rapidly, and all were complete in <45 min. HMPA, a polar aprotic solvent, performed rather sluggishly, and the amount of benzoic acid formed at 60 min was only 46%. Among the more nonpolar solvents, THF gave the best results (completion time 30 min), followed by ethyl acetate (60 min) and 1,4-dioxane (180 min). A reaction with 80% aqueous AcOH (not shown in the table) yielded only 5% benzoic acid, even after 240 min. This poor performance may be due to the involvement of a different donor species, namely formic acid, that prevails in this acidic medium.

Methanol showed the greatest improvement when the catalyst was presaturated with solid ammonium formate. The reaction was complete within 60 min using this method, whereas it was only 30% complete at the same time when the activation period was 1 min. Thus, presaturation was highly beneficial, possibly because of a buildup of the concentration of the active reductive species or due to a solvent-dependent effect on the catalyst surface.

Overall, presaturation did not have a great effect on the course of reaction for the other solvents. When entries 1 and 2 are compared for each solvent, it can be seen that the ethanol reaction improved slightly when presaturated, while reactions with 1-propanol, 2-propanol, and *tert*-butyl alcohol were either unaffected or were slightly worse. Dechlorination with HMPA appeared to be independent of the method of pretreatment. Finally, the reactions involving presaturation proceeded more slowly in THF, 1,4-dioxane, and ethyl acetate.

In Table III, both the substrate and the product are relatively polar. It was also of interest to examine the effect of solvent on the dechlorination of a relatively more lipophilic compound such as 1-chloronaphthalene. In this study, the data were collected only for catalysts that had been presaturated by stirring with solid ammonium formate for 10–20 min.

As Table IV shows, the reactions in all cases except HMPA were much slower than the corresponding reactions in Table III. Thus dehalogenations in EtOH, 1-propanol, 2-propanol, and *tert*-butyl alcohol were complete after 2 h versus 45 min in Table III. In contrast, with HMPA as the solvent, dechlorination of 1-chloronaphthalene proceeded faster than for 2-chlorobenzoic acid and was complete in 4 h. On the other hand, there was no significant difference with 80% aqueous AcOH. Among the nonpolar solvents, EtOAc gave the best result and had noticeably less agglomeration of catalyst than either THF or 1,4-dioxane.

Overall, AF-CTH dehalogenation proceeded faster in alcohols than in the nonpolar solvents for both of the substrates cited above. Among the alcohols themselves, EtOH, the propanols, and *tert*-butyl alcohol were distinctly better than MeOH. While both THF and EtOAc compared favorably with the alcohols in the dechlorination of 2-chlorobenzoic acid, the reaction rates in these solvents were slower when the more lipophilic 1-chloronaphthalene was employed. This may be due to the enhancement in catalyst agglomeration caused by the latter substrate or due to substrate solubility considerations. These results suggest that compounds requiring a nonpolar solvent for dehalogenation would react better either at an elevated temperature or at ambient conditions after dilution with a suitable alcohol.

Applications of Optimized AF-CTH Conditions for Dehalogenation of Mono- and Polychlorinated Aryl Compounds. Analysis of the parameters examined in this study suggests the following conclusions. Among the various supports for Pd, carbon gave the best performance in dechlorination. In addition, a 3% Pd loading appeared to be an efficient choice in terms of cost and reactivity. Reactions proceeded faster in alcohols such as EtOH or 2-propanol, although THF was comparable with moderately hydrophobic substrates. All reactions benefited from an increase in temperature. Finally, a 2-fold excess of ammonium formate was a sufficient quantity of transfer reagent for most dehalogenations.

The dechlorination of a variety of mono- and polychlorinated aryl compounds was performed to evaluate these conclusions, and the results are shown in Table V. The progress of the reactions was followed by RP-HPLC analysis of aliquots taken at 30 and 60 min. Initially, 20 mmol of ammonium formate was added to the substrate containing 10 mmol of chlorine. If the reaction was incomplete at 30 min, an additional 20 mmol of ammonium formate was added.

All the monochlorinated phenols and toluenes were quantitatively reduced in 30 min at room temperature in 2-propanol with 3% Pd/C and a 2-fold excess of ammonium formate. Similarly, 2,4-dichlorobenzoic acid and 2,4-dichlorotoluene were converted to benzoic acid and toluene in 60 and 30 min, respectively. While the reaction of 2,5-dichloro-*p*-xylene and 1,2,3,4-tetrachlorobenzene were performed in refluxing 2-propanol, THF was employed for the more hydrophobic 2,3,5,6-tetrachloro-*p*-xylene. A partial consideration for electing a refluxing medium was the enhanced solubility of the substrate. Overall, the results augment our conclusions and demonstrate that facile dechlorination reactions are achievable under ambient conditions with a wide variety of aryl chlorides.

Experimental Section

Ammonium formate was purchased from Sigma. Substrates were purchased from Aldrich or were of reagent grade from other commercial sources. The catalysts 5% Pd/Al_2O_3 and 5% Pd/$CaCO_3$ were purchased from Pfaltz and Bauer. The 5% Pd/kieselguhr was obtained from Aesar, and the 10% Pd/Al_2O_3 was obtained from Alfa. All other catalysts were purchased from Aldrich.

RP-HPLC analyses were performed on a Hitachi L-5000 system equipped with a D-2000 integrator. Columns employed were a 4.6 × 250 mm Phenomenex Ultracarb 5 C-30 and a 4.6 × 250 mm Hibar C-18 ODS. Solvents were analytical or HPLC grade. The conditions of chromatography for the various analyses are footnoted at the respective tables.

Table V. Ammonium Formate Catalytic Transfer Hydrogenolysis of Aryl Chlorides in the Presence of 3% Pd/C Catalyst[a]

substrate	reaction time,[a] min	solvent[c]	product[d]	HPLC parameters: t_R (substrate), min	HPLC parameters: t_R (product), min	system[e]
2-chlorophenol	30	2-propanol	phenol	14.92	6.46	I
3-chlorophenol	30	2-propanol	phenol	16.75	6.42	I
4-chlorophenol	30	2-propanol	phenol	16.60	6.40	I
2-chlorotoluene	30	2-propanol	toluene	5.26	3.67	II
3-chlorotoluene	30	2-propanol	toluene	5.27	3.68	II
4-chlorotoluene	30	2-propanol	toluene	5.18	3.66	II
1-chloronaphthalene	30	2-propanol (reflux)	naphthalene	7.32	4.90	III
2,4-dichlorobenzoic acid	60	2-propanol	benzoic acid	15.81	8.74	IV
2,4-dichlorotoluene	30	2-propanol	toluene	8.90	3.72	II
2,5-dichloro-*p*-xylene	30	2-propanol (reflux)	*p*-xylene	9.04	5.22	V
1,2,3,4-tetrachlorobenzene	30	2-propanol (reflux)	benzene	11.08	2.80	VI
2,3,5,6-tetrachloro-*p*-xylene	30	THF (reflux)	*p*-xylene	16.06	5.22	V

[a] Reaction conditions: 3% Pd/C (0.50 g) + solvent (50 mL) + $NH_4^+HCOO^-$ (2.52 g; 40 mmol) in H_2O (2 mL) + substrate (Cl content, 10 mmol). [b] Reaction times given are for quantitative dehalogenation and are not optimized. Aliquots were removed at 30-min intervals and assayed by RP-HPLC. [c] All reactions were done at ambient temperature and pressure unless otherwise noted. [d] Product identity confirmed by chromatographic comparison with authentic samples. [e] System I: Hibar ODS column. Aqueous phase (A) = water containing AcOH (pH = 2.5); organic phase (B) = methanol. An isocratic gradient of 10% B for 8 min followed by a linear gradient of 10–70% B over 10 min at a flow rate of 2 mL/min (λ = 256 nm). System II: Hibar ODS column. A = H_2O; B = MeOH. A linear gradient of 70–75% B over 10 min at 2 mL/min (λ = 256 nm). System III: Hibar ODS column. A = H_2O; B = MeOH. A linear gradient of 70–100% B over 20 min at 2 mL/min (λ = 254 nm). System IV: Hibar ODS column. A = H_2O/H_3PO_4 (pH = 1.5); B = MeOH. Mobile phase composition was changed from 30 to 70% B over 20 min, while changing the flow from 1.5 to 2.0 mL/min. (λ = 256 nm). System V: Phenomenex 5-ODS-30. A = H_2O; B = MeOH. A linear gradient of 85–100% B over 15 min at 2 mL/min (λ = 254 nm). System VI: Hibar ODS column. A = H_2O, B = MeOH. A combination linear gradient of 70–75% B over 5 min and 75–100% B over 15 min at 2 mL/min (λ = 254 nm).

AF-CTH of 4-Chloroanisole with Various Supports (Table I). To a 100-mL round-bottom flask were added *x*% Pd/support (0.5 g, *x* = 5 or 10), a chip of dry ice, 2-propanol (25 mL), and a stir bar. The flask was then placed in a water bath to maintain a constant temperature. Next was added a solution of ammonium formate (2.52 g, 40.0 mmol) in H_2O (2 mL), and stirring was begun. After 1 min, 4-chloroanisole (1.23 mL, 10.0 mmol) was added. Aliquots were removed at 5, 10, 20, 30, 45, 60, and 120 min.

Effect of Temperature on AF-CTH Dehalogenation (Table II). To 0.5 g of catalyst in a 100-mL round-bottom flask were added water (2 mL) and alcohol (20 mL). The suspension was either stirred at room temperature or at reflux. Next, aryl chloride (10 mmol) dissolved in THF (2 mL) and solid ammonium formate (5 g) was added. Reaction aliquots were removed at periodic intervals (5, 10, 15, 20, 30, 45, 60, 90, and 120 min) and assayed by RP-HPLC. In the case of 2-chlorobenzoic acid, 1% Pd/C granules (1.5 g) and a further 40 mmol of ammonium formate in water (2.0 mL) were used.

AF-CTH of 2-Chlorobenzoic Acid (Table III). A. Presaturation. To a 100-mL round-bottom flask were added 3% Pd/C (0.50 g), a chip of dry ice, solvent (25 mL), and a stir bar. The flask was then placed in a water bath to maintain a constant temperature (20 ± 2 °C). Ammonium formate (2.52 g, 40 mmol) was then added, and stirring was begun. After about 20 min, a solution of ammonium formate (2.52 g, 40 mmol) in H_2O (2 mL) was added. One minute later, a solution of 2-chlorobenzoic acid (1.56 g, 10.0 mmol) in solvent (25 ml) was added. Aliquots were removed at 5, 10, 20, 30, 45, 60, 180, and 240 min.

B. One-Minute Activation. To a 100-mL round-bottom flask were added 3% Pd/C (0.50 g), a chip of dry ice, solvent (25 mL), and a stir bar. The flask was then placed in a water bath to maintain a constant temperature. A solution of ammonium formate (2.52 g, 40.0 mmol) in H_2O (2 mL) was then added. After 1 min, 2-chlorobenzoic acid (1.56 g, 10.0 mmol) in solvent (25 mL) was added. Aliquots were removed at 5, 10, 20, 30, 45, 60, 120, and 180 min.

AF-CTH of 1-Chloronaphthalene (Table IV). To a 100-mL round-bottom flask were added 3% Pd/C (0.50 g), a chip of dry ice, solvent (50 mL), and a stir bar. The flask was then placed in a water bath to maintain a constant temperature. After stirring was begun, solid ammonium formate (2.52 g, 40.0 mmol) was added. The mixture was stirred further until effervescence began. Next was added ammonium formate (2.52 g, 40.0 mmol) in H_2O (2 mL). After 1 min, 1-chloronaphthalene (1.36 mL, 10.0 mmol) was added. Aliquots were removed at 5, 10, 20, 30, 45, 60, and 120 min.

AF-CTH of Aryl Chlorides (Table V). To a 250-mL round-bottom flask were added 3% Pd/C (0.50 g), a chip of dry ice, 2-propanol (40 mL), and a stir bar. Stirring was begun, and the mixture was brought to reflux. Next was added half of a solution of ammonium formate (2.52 g, 40.0 mmol) in H_2O (2 mL), followed by a solution of 2,5-dichloro-*p*-xylene (0.87 g, 5.0 mmol) in 2-propanol (10 mL). The remaining ammonium formate solution was added after 30 min. Aliquots were removed at 30 and 60 min. A similar procedure was used for the remaining entries.

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Registry No. 4-Chloroanisole, 623-12-1; ammonium formate, 540-69-2; anisole, 100-66-3; 2-chlorotoluene, 95-49-8; toluene, 108-88-3; 4-chlorotoluene, 106-43-4; 1-chloronaphthalene, 90-13-1; naphthalene, 91-20-3; 2-chlorobenzoic acid, 118-91-2; benzoic acid, 65-85-0; 2-chlorophenol, 95-57-8; phenol, 108-95-2; 3-chlorophenol, 108-43-0; 4-chlorophenol, 106-48-9; 3-chlorotoluene, 108-41-8; 2,4-dichlorobenzoic acid, 50-84-0; 2,4-dichlorotoluene, 95-73-8; 2,5-dichloro-*p*-xylene, 1124-05-6; *p*-xylene, 106-42-3; 1,2,3,4-tetrachlorobenzene, 634-66-2; benzene, 71-43-2; 2,3,5,6-tetrachloro-*p*-xylene, 877-10-1.