Transition Metal Complex Catalyzed Carbonylation of Organic Halides in *N,N,N',N'*-Tetraalkylurea Solution in the Absence of Added Base

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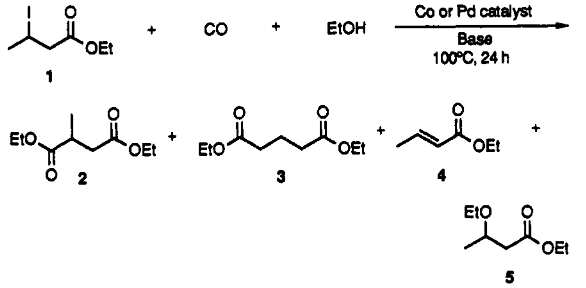
Introduction

How to replace the halogen atom of an alkyl halide with another functional group by means of a transition metal catalyzed reaction remains an unsolved problem.[1] Usually, the desired transformation does not proceed because alkyl halides (e.g. $R^1CH_2CH_2X$; X = halogen atom) oxidatively add to low-valent transition metal complexes (Met) only slowly, and furthermore, β-elimination reaction of metal halohydride (H-Met-X) from the oxidative adducts, σ-alkylmetal–halo complexes ($R^1CH_2CH_2$-Met-X), may occur preferentially to afford olefins ($R^1CH{=}CH_2$).[2]

Recently, we reported that the carbonylation of alkyl iodides bearing a perfluoroalkyl group at the β-position ($R_fCH_2CH(R)I$) is catalyzed by Co, Rh, or Pd complexes in the presence of a base to give, in moderate to good yield, carboxylic acids or esters without any side reactions.[3] These results encouraged us to examine the carbonylation of alkyl halides bearing other functional groups.

Results and Discussion

The carbonylation of ethyl 3-iodobutanoate (1) was attempted first. If 1 could oxidatively add to a low-valent transition metal complex, its carbonyl oxygen atom should be in a position to coordinate with the central metal atom of the complex (A) to form a five-membered ring, as shown in Figure 1. Such intramolecular coordination would inhibit β-hydride elimination from the intermediate A. Initially, the Co- or Pd-catalyzed carbonylation of 1 was attempted in ethanol solution in the presence of a base like K_2CO_3, Et_3N, $^iPr_2EtN$, or KF (normal Heck's carbonylation conditions)[4] under 50 atm of carbon monoxide pressure at 100 °C for 24 h. However, contrary to expectation, ethyl crotonate (4) was formed exclusively. No carbonylated products were obtained. The Pd-catalyzed carbonylation of 1 in the presence of pyridine afforded the desired diethyl 2-methylsuccinate (2) and diethyl pentanedioate (3), in 41% and 14% yield, respectively. Ester 4 (32%) and ethyl 3-ethoxybutanoate (5, 7%) were byproducts. The role of base in Heck-type carbonylations is to trap the hydrogen halide produced in the catalytic cycle. The results described above showed that the base directly attacks the hydrogen atom α to the carbonyl group of 1. This results in the elimination of hydrogen iodide prior to the oxidative addition of 1 to the low-valent transition metal catalyst. It was concluded that base-free or very weakly basic conditions were necessary to effect the carbonylation of 1 in satisfactory yield.



(1)

Because aprotic polar solvents are good proton acceptors, the carbonylation of 1 in such solvent in the absence of added base was examined. The results are summarized in Table I. The yield of the desired product (2) increased dramatically when the $(Ph_3P)_2PdCl_2$-catalyzed carbonylation was performed in *N,N,N',N'*-tetramethylurea (TMU). These results indicated that TMU is the solvent that most effectively suppresses elimination of HI from the starting material (1) or β-elimination of metal halohydride from the intermediate A.

To determine how generally applicable the reaction conditions were, the carbonylation of representative alkyl, allyl, benzyl, aryl, and vinyl halides was attempted. A stainless steel autoclave containing a mixture of organic halide (1 mmol), an alcohol or H_2O (10 mmol), Pd (2–5 mol %), or Co (10 mol %) catalyst[5] and solvent (1.4 mL) was pressurized to 30–50 atm with carbon monoxide pressure and then was heated at 100 °C for 24 h. Representative results are shown in Table II. When *primary* alkyl halides were employed as starting materials (entires 1–8), $Co_2(CO)_8$-catalyzed carbonylation gave the desired products in better yields than did $(Ph_3P)_2PdCl_2$-catalyzed reaction. However, $(Ph_3P)_2PdCl_2$ was the catalyst of choice when *secondary* alkyl halides were used (entries 9–12). The formation of alkenes or alkanes from the alkyl halides (entries 1–12) was not observed (GLC analysis). This indicated that β-hydride elimination and reduction of the intermediate σ-alkylmetal species did not occur under the reaction conditions employed. Alkyl ethyl ethers, which can be formed by the reaction of the alkyl halide and ethanol at 100 °C in TMU in the absence of a catalyst, were also obtained in low yields as byproducts. It is noteworthy that other *N,N,N',N'*-tetraalkylureas, 1,3-dimethyl-2-imidazolidinone (DMI), and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU), are also effective solvents for effectintg carbonylation in the absence of added base. Carboxylic acids could be also synthesized, in good yield, by the Co- or Pd-catalyzed carbonylation of alkyl halides in the presence of H_2O in *N,N,N',N'*-tetraalkylurea solution (entries 4 and 11). Interestingly, a mixture of regioisomeric esters was obtained from *secondary* alkyl iodides like ethyl 3-iodobutanoate (eq 1) and 2-iodooctane (entry 12). This results indicates that the insertion of CO into the initially formed *sec*-alkylmetal intermediate and isomerization of the *sec*-alkylmetal intermediate to an *n*-alkylmetal species are competitive reactions. Not only aliphatic iodides or bromides but also benzyl, allyl, aryl, and vinyl halides can be used as starting materials. In *N,N,N',N'*-tetraalkylurea solution, the carbonylation of aryl iodides in the presence

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[1] (a) Sustmann, R.; Lau, J.; Zipp, M. *Tetrahedron Lett.* **1986**, *27*, 5207. (b) Takeuchi, R.; Tsuji, Y.; Watanabe, Y. *J. Chem. Soc., Chem. Commun.* **1986**, 351. (c) Takeuchi, R.; Tsuji, Y.; Fujita, M.; Kondo, T.; Watanabe, Y. *J. Org. Chem.* **1989**, *54*, 1831. (d) Kondo, T.; Tsuji, Y.; Watanabe, Y. *Tetrahedron Lett.* **1988**, *29*, 3833. (e) Castle, P. L.; Widdowson, D. A. *Tetrahedron Lett.* **1986**, *27*, 6013. (f) Yuan, K.; Scott, W. J. *Tetrahedron Lett.* **1989**, *30*, 4779.

[2] (a) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987. (b) Yamamoto, A. *Organotransition Metal Chemistry*; John Wiley & Sons, Inc.: New York, 1986. (c) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.

[3] (a) Urata, H.; Kosukegawa, O.; Ishii, Y.; Yugari, H.; Fuchikami, T. *Tetrahedron Lett.* **1989**, *30*, 4403. (b) Urata, H.; Ishii, Y.; Fuchikami, T. *Tetrahedron Lett.* **1989**, *30*, 4407.

[4] Heck, R. F. *Palladium Reagents in Organic Syntheses*; Academic Press: New York, 1985.

[5] When various Rh, Ru, Ni, and Pt[1b-d] complexes were used as catalysts, the desired carbonylated products were obtained only in low yield.

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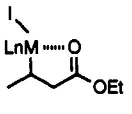


A

Figure 1. Postulated oxidative adduct A.

Table I. $(Ph_3P)_2PdCl_2$-Catalyzed Carbonylation of Ethyl 3-Iodobutanoate (1) in Aprotic Polar Solvents[a]

entry	solv (mL)	EtOH, mL	% yield 2	3	4	5
1[b]	CH_3CN (1.4)	0.6	15	1	4	4
2[c]	DMF (1.4)	0.6	20	5	15	3
3	HMPA (1.4)	0.6	31	6	44	1
4	TMU (1.4)	0.6	71	5	5	3

[a] All reactions were performed under 50 atm of CO at 100 °C for 24 h. [b] Starting material (1) was recovered in 55% yield. [c] Many unidentified products were also formed.

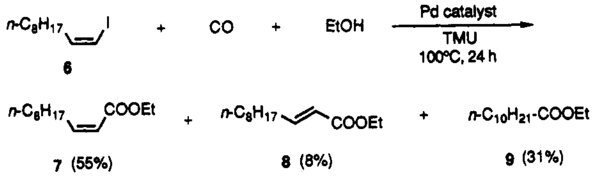
Table II Carbonylation of Organic Halides in *N,N,N′,N′*-Tetraalkylurea Solution[a]

$$RX + CO + HY \xrightarrow[\text{solvent}\ 100\,°C,\ 24\ h]{\text{catalyst}} RCOY$$

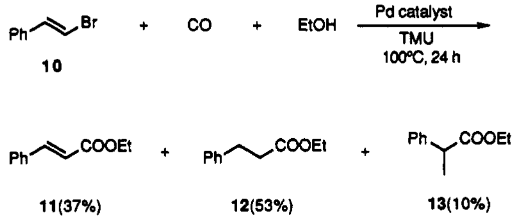
entry	R-X	CO, atm	HY	solv	catalyst[b] (mol %)	% yield
1	n-C_8H_{17}-I	50	EtOH	TMU	Co (10)	86 (1)[c]
2	n-C_8H_{17}-I	50	EtOH	DMI	Co (10)	67 (5)[c]
3	n-C_8H_{17}-I	50	EtOH	DMPU	Co (10)	84 (5)[c]
4	n-C_8H_{17}-I	50	H_2O	TMU	Co (10)	97[d]
5	n-C_8H_{17}-Br	50	EtOH	TMU	Co (10)	61 (6)[c]
6	n-$C_{10}H_{21}$-I	50	EtOH	DMPU	Co (10)	88
7	$MeO(CH_2)_3$-I	50	MeOH	TMU	Co (10)	91
8	MeOCO-$(CH_2)_2$-I	50	MeOH	TMU	Co (10)	65
9	c-C_6H_{11}-I	50	EtOH	TMU	Pd (5)	70
10	c-C_6H_{11}-I	50	EtOH	DMPU	Pd (5)	70
11	c-C_6H_{11}-I	50	H_2O	TMU	Pd (5)	76[d]
12	n-C_6H_{13}CH-(CH_3)-I	50	EtOH	DMI	Pd (5)	51[e] (5)[c]
13	2-cyclohexenyl-Br	30	EtOH	TMU	Pd (2)	77
14	$PhCH_2$-Br	50	EtOH	TMU	Pd (5)	84
15	$PhCH_2$-Br	50	EtOH	TMU	Co (10)	76
16	$PhCH_2$-Cl	50	EtOH	TMU	Pd (5)	47 (22)[c]
17	1-Naph-I	30	EtOH	TMU	Pd (2)	99
18	p-HOC_6H_4-I	30	EtOH	TMU	Pd (2)	99
19	o-MeC_6H_4-I	30	EtOH	DMI	Pd (2)	92
20	p-CH_3CO-C_6H_4-I	30	EtOH	DMPU	Pd (2)	85

[a] All reactions were performed in a stainless steel autoclave containing a mixture of the organic halide (1 mmol), HY (10 mmol), Co or Pd catalyst, and solvent (1.4 mL) under 30–50 atm of CO pressure at 100 °C for 24 h. [b] Co = $Co_2(CO)_8$; Pd = $(Ph_3P)_2PdCl_2$. [c] The corresponding alkyl ethyl ether was also obtained, in the yield shown in parentheses. [d] The yield was estimated by GLC analysis of the corresponding methyl ester, which was prepared by treating the carboxylic acid with CH_2N_2/Et_2O. [e] Ethyl nonanoate was also produced, in 9% yield.

of Pd complexes[6] took place under 30 atm of CO pressure in excellent yield in the absence of added base.[7] Furthermore, a mixture of unsaturated and saturated esters was obtained from the carbonylation of vinyl halides like (*Z*)-1-iodo-1-decene (**6**, eq 2) and β-bromostyrene (**10**, eq 3) under the same reaction conditions (Table II). It is not yet clear why saturated esters like **9**, **12**, and **13** were obtained. That ester **13** was formed suggests that the reductive dehalogenation of the vinyl halide to an alkene occurs first, and subsequent hydroesterification affords the saturated ester.



(2)



(3)

As has been shown here, *N,N,N′,N′*-tetraalkylureas like TMU, DMPU, and DMI are good solvents for the transition metal complex catalyzed carbonylation of various organic halides, even in the absence of an added base. Further investigation of the transition metal complex catalyzed reactions of organic halides under base-free conditions is in progress.

Experimental Section

^{1}H NMR spectra were recorded at 90 and 400 MHz with Hitachi R-90H and Brucker AM-400 spectrometers, respectively. Chemical shifts are reported in ppm downfield from Me_4Si (δ) and were in reference to Me_4Si in $CDCl_3$. ^{13}C NMR spectra were recorded at 100 MHz with a Brucker AM-400 spectrometer. Chemical shifts are reported in ppm downfield from internal Me_4Si (δ). IR spectra were recorded with a JASCO A-202 spectrometer. Mass spectra were recorded with a Hitachi RMU-6MG spectrometer at an ionization voltage of 70 eV. GLC analyses were performed with a Shimadzu GC-7A chromatograph equipped with a 3 mm × 1 m glass columns packed with either 30% SE-30 on 60–80-mesh Uniport B or 30% DC-550 on 60–80-mesh Uniport B.

The *N,N,N′,N′*-tetraalkylureas TMU, DMI, and DMPU were used as received. CH_2Cl_2 was distilled from CaH_2 under Ar immediately before use.

Ethyl 3-iodobutanoate (1), 2-iodooctane, and 3-methoxy-1-iodopropane were prepared from the corresponding alcohols.[8]

General Procedure. Pd-catalyzed carbonylation. A stirred mixture of ethyl 3-iodobutanoate (1, 152 μL, 1 mmol), $(Ph_3P)_2PdCl_2$ (35.2 mg, 0.05 mmol), EtOH (0.6 mL, 10 mmol), and *N,N,N′,N′*-tetramethylurea (TMU, 1.4 mL) was heated at 100 °C for 24 h under 50 atm of CO pressure in a 10-mL stainless steel autoclave (Taiatsu Scientific Glass Co., Ltd., SUS 316). When the reaction was complete, the mixture was acidified with 3 N aqueous HCl and was then extracted with Et_2O. The Et_2O extract was washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel ($CHCl_3$) to give a mixture (148.4 mg) of diethyl 2-methylsuccinate (**2**), diethyl pentanedioate (**3**), and ethyl 3-ethoxybutanoate (**5**). Analysis by ^{1}H NMR, GLC, and GC–MS showed that **2** was the major product (71% yield) and **3** (5%) and **5** (3%) were byproducts.

2: ^{1}H NMR ($CDCl_3$) δ 1.22 (d, J = 7.2 Hz, 3 H), 1.25 (t, J = 7.0 Hz, 3 H), 1.26 (t, J = 7.0 Hz, 3 H), 2.39 (dd, J = 16.4 and 6.1 Hz, 1 H), 2.72 (dd, J = 16.4 and 8.1 Hz, 1 H), 2.90 (ddq, J = 8.1, 6.1, and 7.2 Hz, 1 H), 4.13 (q, J = 7.0 Hz, 2 H), 4.15 (q, J = 7.0

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[6] The carbonylation of iodobenzene catalyzed by Pd(II) complexes bearing phosphine ligands like PPh_3, PEt_3, PMe_3, dppe, dppp, and dppb was investigated. Among these complexes, $(Ph_3P)_2PdCl_2$ showed the highest catalytic activity and gave ethyl benzoate in 82% yield.

[7] The $(Ph_3P)_2PdCl_2$-catalyzed carbonylation of iodobenzene in the presence of ethanol and in the absence of added base was also performed in other solvents. The yield of ethyl benzoate as a function of the solvent was as follows: EtOH, 27%; benzene, 18%; THF, 31%; acetone, 42%; CH_3CN, 30%; DMF, 5%; DMSO, 2%; and HMPA, 42%.

[8] (a) Eglinton, G.; Whiting, M. C. *J. Chem. Soc.* **1950**, 3650. (b) House, H. O.; Lord, R. C.; Rao, H. S. *J. Org. Chem.* **1956**, *21*, 1487.

J. Org. Chem. 1991, 56, 4322-4325

Hz, 2 H); ^{13}C NMR (CDCl$_3$) δ 14.16, 14.18, 17.01, 35.88, 37.74, 60.60, 77.22, 171.80, 175.23; IR (neat) 1737 cm^{-1} (ν(C=O)); MS *m/e* 143 (97), 115 (100), 87 (47), 73 (36), 45 (31), 29 (93).

3: ^{1}H NMR (CDCl$_3$) δ 1.26 (t, *J* = 7.1 Hz, 6 H), 1.95 (tt, *J* = 7.4 and 7.4 Hz, 2 H), 2.36 (t, *J* = 7.4 Hz, 4 H), 4.13 (q, *J* = 7.1 Hz, 4 H); IR (neat) 1740 cm^{-1} (ν(C=O)); MS *m/e* 143 (100), 115 (73), 114 (59), 87 (53), 55 (31), 45 (23), 42 (31), 29 (75).

5: MS *m/e* 131 (25), 116 (33), 115 (23), 73 (100), 45 (100), 29 (84).

Co-Catalyzed Carbonylation. A stirred mixture of Co$_2$(CO)$_8$ (34.0 mg, 0.10 mmol), 1-iodooctane (181 μL, 1.0 mmol), EtOH (0.6 mL, 10 mmol), and TMU (1.4 mL) in a 10-mL stainless steel autoclave was heated at 100 °C for 24 h under 50 atm of CO. The mixture was made slightly acidic and was extracted with Et$_2$O. The extract was washed with water and dried (MgSO$_4$). The extract was concentrated, and the residue was purified by flash chromatography to provide a mixture (161.0 mg) of ethyl nonanoate and ethyl octyl ether. ^{1}H NMR analysis showed that ethyl nonanoate was formed in 86% yield and ethyl octyl ether in 1% yield.

Ethyl nonanoate: ^{1}H NMR (CDCl$_3$) δ 0.88 (bt, 3 H), 1.27 (t, *J* = 7.0 Hz, 3 H), 1.10–1.80 (br, 12 H), 2.32 (t, *J* = 7.0 Hz, 2 H), 4.16 (q, *J* = 7 Hz, 2 H); ^{13}C NMR (CDCl$_3$) δ 14.08, 14.27, 22.64, 25.00, 29.12, 29.16, 29.23, 31.81, 34.41, 60.13, 173.86; IR (neat) 1744 cm^{-1} (ν(C=O)); MS *m/e* 186 (M$^+$, 1), 141 (12), 101 (34), 88 (100), 73 (25), 71 (13), 70 (18), 69 (12), 61 (30), 60 (34), 57 (30), 55 (30), 45 (20), 43 (37), 41 (65), 39 (19), 29 (93).

Ethyl octyl ether: ^{1}H NMR (CDCl$_3$) δ 0.89 (bt, 3 H), 1.1–1.8 (m, 15 H), 3.42 (t, *J* = 7.0 Hz, 2 H), 3.48 (t, *J* = 7.0 Hz, 2 H); MS *m/e* 112 (7), 84 (23), 83 (13), 59 (100), 57 (19), 56 (31), 47 (30), 42 (18), 41 (38), 31 (81), 29 (42).

For products other than those listed above, all the spectroscopic (^{1}H and ^{13}C NMR, and IR) data were identical with those of authentic samples.

Difluoromethylation of Alkenes via Borohydride Reduction of 1,3-Dibromo-1,1-difluoroalkanes

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The synthesis of difluoromethyl-substituted compounds has been an area of active interest, as many of these compounds have been found to be biologically active.[1] The difluoromethyl group has been classically prepared by geminal difluorination of a corresponding aldehyde.[2,3] More recently the use of fluorinated building blocks in synthesis has gained increasing popularity, and methods involving these are being reported for the synthesis of functionalized, difluoromethyl-substituted compounds.[4-6]

In the course of investigating the reactions of 1,3-dibromo-1,1-difluoroalkanes 2 with various nucleophiles,[7,8] we have found that these compounds undergo selective reduction of one or both carbon–bromine bonds upon treatment with sodium borohydride in DMSO.[9-12] In the

Scheme I

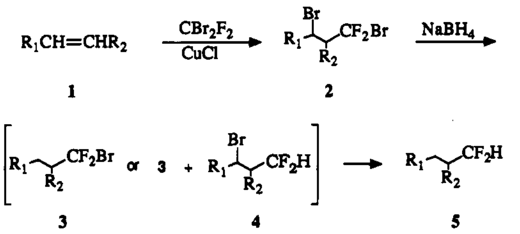
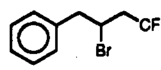
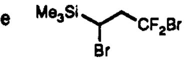
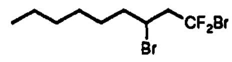
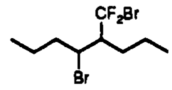
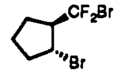
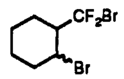
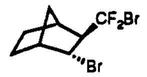


Table I. Yields of Dibromides 2, Bromides 3, and *gem*-Difluoroalkanes 5

			% yield[a]		
	starting alkene, 1	CBr$_2$F$_2$ adduct, 2	2	3	5
1a	allylbenzene		32	74	(30)
1b	vinyltrimethylsilane		58	61	29
1c	1-octene		77	34	57
1d	*trans*-4-octene		50	12	38
1e	cyclopentene		31		(21)
1f	cyclohexene		51		27
1g	norbornene		76		(48)

[a] Isolated yields based on starting material charged. Parentheses denote GC or crude yields.

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(1) (a) Filler, R.; Kobayashi, Y. *Biomedicinal Aspects of Fluorine Chemistry*; Kodansha, Elsevier Biomedical: Tokyo, 1983. (b) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123. (c) Walsh, C. *Tetrahedron* **1982**, *38*, 871.

(2) A wide range of fluorinating agents has been used for this transformation. Some of these include: (a) DAST (diethylamino)sulfur trifluoride): Middleton, W. J. *J. Org. Chem.* **1975**, *40*, 574. For a review, see: Hudlicky, M. *Org. React.* **1988**, *35*, 513–637. (b) SF$_4$: Boswell, G. A.; Ripka, W. C.; Scribner, R. M.; Tullock, C. W. *Org. React.* **1974**, *21*, 1. Also, see: Dmowski, W. *J. Fluorine Chem.* **1986**, *32*, 255. (c) SeF$_4$: Olah, G. A.; Nojima, M.; Kerekes, I. *J. Am. Chem. Soc.* **1974**, *96*, 925. (d) MoF$_6$: Mathey, F.; Bensoam, J. *Tetrahedron* **1971**, *27*, 3965. (e) Phenylsulfur trifluoride: Sheppard, W. A. *J. Am. Chem. Soc.* **1962**, *84*, 3058.

(3) This conversion has also been effected in two steps via the intermediate 1,3-dithiolanes (Sondej, S. C.; Katzenellenbogen, J. A. *J. Org. Chem.* **1986**, *51*, 3508) or hydrazones (Rozen, S.; Brand, M.; Zamir, D.; Hebel, D. *J. Am. Chem. Soc.* **1987**, *109*, 896).

(4) For example, some enolate carbanions can be alkylated with CHClF$_2$ (via insertion of difluorocarbene): (a) Bey, P.; Gerhart, F.; Dorsselaer, V. V.; Danzin, C. *J. Med. Chem.* **1983**, *26*, 1551. (b) Tsushima, T.; Kawada, K.; Ishihara, S.; Uchida, N.; Shiratori, O.; Higaki, J.; Hirata, M. *Tetrahedron* **1988**, *44*, 5375. (c) Bey, P.; Vevert, J. P.; Dorsselaer, V. V.; Kolb, M. *J. Org. Chem.* **1979**, *44*, 2732.

(5) For examples involving the hydrogenation of difluoromethylene derivatives, see: (a) α-Difluoromethyl carboxylic acids: Kitazume, T.; Ohnogi, T.; Miyauchi, H.; Yamazaki, T.; Watanabe, S. *J. Org. Chem.* **1989**, *54*, 5630. (b) Motherwell, W. B.; Tozer, M. J.; Ross, B. C. *J. Chem. Soc., Chem. Commun.* **1989**, *19*, 1437.

(6) Other examples include: (a) Allylic difluoromethyl compounds: Hartgraves, G. A.; Burton, D. J. *J. Fluorine Chem.* **1988**, *39*, 425. (b) α-Difluoromethyl alcohols: Stahly, G. P. *J. Fluorine Chem.* **1989**, *43*, 53. (c) α-Difluoromethyl ketones: Ichikawa, J.; Sonoda, T.; Kobayashi, H. *Tetrahedron Lett.* **1989**, *30*, 5437.

(7) For a review on the free-radical addition of dibromodifluoromethane to alkenes, see: Sosnovsky, G. *Free Radical Reactions in Preparative Organic Chemistry*; Macmillian: New York, 1964; Chapter 2, pp 42–44.

(8) The CF$_2$Br$_2$–alkene adducts react with some nucleophiles via elimination–addition chemistry, often resulting in facile dehalogenations to give α,β-unsaturated carbonyl compounds: (a) Elsheimer, S.; Michael, M.; Landavazo, A.; Slattery, D. K.; Weeks, J. *J. Org. Chem.* **1988**, *53*, 6151. (b) Elsheimer, S.; Slattery, D. K.; Michael, M.; Weeks, J.; Topoleski, K. *Ibid.* **1989**, *54*, 3992.

(9) For a review on the dehalogenation of halofluoroalkanes, see: Mettille, F. J.; Burton, D. J. *Fluorine Chem. Rev.* **1967**, *1(2)*, 315. For a review on the reduction of alkyl halides in general, see: Pinder, A. R. *Synthesis* **1980**, 425.

(10) Sodium borohydride in polar, aprotic solvents has been proposed as a reagent for the reduction of alkyl halides: (a) Hutchins, R. O.; Kandasamy, D.; Dux, F.; Maryanoff, C. A.; Rotstein, D.; Goldsmith, B.; Burgoyne, W.; Cistone, F.; Dalessandro, J.; Puglis, J. *J. Org. Chem.* **1978**, *43*, 2259. (b) Bell, H. M.; Vanderslice, C. W.; Spehar, A. *Ibid.* **1969**, *34*, 3923.

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