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Mild, Selective, General Method of Ketone Synthesis from Acid Chlorides and Organotin Compounds Catalyzed by Palladium

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Benzylchlorobis(triphenylphosphine)palladium(II) catalyzes the reaction of acid chlorides with tetraorganotin compounds to give ketones in quantitative yields. The reaction is general with respect to both reactants, and a wide variety of substituent groups on the acid chloride, including an aldehyde function, is tolerated, thus making this reaction one of the most general methods for ketone synthesis. The reaction is accelerated by oxygen, deactivated by triphenylphosphine, and shows an abnormal dependence on catalyst concentration. Benzoylchlorobis(triphenylphosphine)palladium(II), a key intermediate in the catalytic cycle, has been shown to react with tetramethyltin to afford acetophenone. The mechanism of the catalytic reaction is discussed.

Syntheses of a number of ketones using organometallic reagents suffer from a variety of unwanted side reactions, the major one of which is the addition of the organometallic reagent to the product ketone. Transition-metal catalyzed coupling reactions of acid halides with organometallic reagents have received considerable attention recently;[1-3] we have discovered a general and selective method for the quantitative synthesis of ketones from acid chlorides and organotin compounds[4] (eq 1).

$$\mathrm{RCOCl} + \mathrm{R'_4Sn} \xrightarrow[\text{HMPA, 65 °C}]{\mathrm{PhCH_2Pd(PPh_3)_2Cl\ (1)}} \mathrm{RCOR'} + \mathrm{R'_3SnCl} \qquad (1)$$

Results and Discussion

Reaction 1 is general both with respect to the organotin compound and the acid chloride (Table I). Aromatic, aliphatic, and heterocyclic acid chlorides have been utilized (section 1, Table I). Sterically hindered acid chlorides react normally (entries 1f and 2f), and α,β-unsaturated acid chlorides (entries 1c and 1g) do not undergo conjugate addition. Diacid chlorides can also be utilized (entries 1h and 1i), with the exception of oxalyl chloride, which reacts with tetramethyltin in the presence of 1 to yield small amounts (10%) of acetone instead of the expected diacetyl. Acetone is probably formed in this reaction by decarbonylation of the intermediate monoacid chloride (eq 2). The liberated carbon monoxide can react with the intermediate Pd(0) complex to form unreactive palladium carbonyl complexes.

$$\mathrm{ClC(=O)C(=O)Cl} \xrightarrow{\mathrm{Me_4Sn}} \mathrm{CH_3C(=O)C(=O)Cl} \xrightarrow{-\mathrm{CO}} \mathrm{ClCCH_3} \longrightarrow \mathrm{CH_3CCH_3} \qquad (2)$$

There is no further addition to the product ketone, while this is the major side reaction when other organometallic reagents (cadmium, zinc, magnesium) are utilized; low temperatures are generally required to avoid this reaction when organocopper compounds are used.[5] Reaction 1 can be carried out in the presence of a wide variety of functional groups. Nitro, nitrile, arylhalo, methoxy, ester, and *even aldehyde functions are tolerated.* This feature, combined with the fact that the reaction is performed under neutral conditions, made the synthesis of *p*-acetylbenzaldehyde possible. Difficulties are encountered in the preparation of this compound by other methods due to the propensity for self-condensation under conditions which are not strictly neutral.[6,7] However, bromine substituents in a position affected by electron-withdrawing groups compete with the acyl chloride for the tin compound (entry 2d).

Since in most cases there are virtually no side reactions that complicate isolation and purification, the yields are high and the workup is simple. The solvent and trimethyltin chloride are removed by water extraction, and the product is purified by distillation or crystallization. In cases where water-insoluble triorganotin chlorides are formed, the product can be separated from the tin compound by distillation or alternatively the triorganotin chlorides can be converted into the highly insoluble triorganotin fluorides by addition of an alcoholic solution of potassium fluoride to the ethereal solution of the product. The end of the reaction is clearly visualized since palladium metal precipitates as soon as all of the acid chloride is consumed and the clear yellow solution turns black. The manipulation is very simple, and there is no need for an inert atmosphere; on the contrary, oxygen has an accelerating effect on the reaction (vide infra).

Almost any tetraorganotin compound can be utilized for reaction 1 (Table I, section 3). Triorganotin chlorides also react (entry 3h), or alternatively a second organic group can also be transfered from tetraorganotin compounds. However, this transfer is much slower than transfer of the first organic

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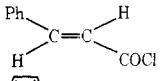
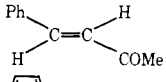
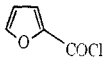
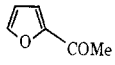
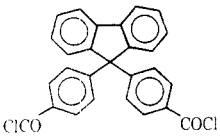
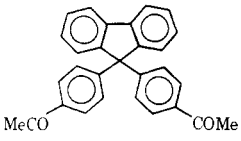
Table I. Synthesis of Ketones from RCOCl and R'_4Sn

entry	RCOCl	registry no.	R'_4Sn	registry no.	RCOR'	registry no.	yield[a] of RCOR', %
1a	$PhCOCl$	98-88-4	Me_4Sn	594-27-4	$PhCOMe$	98-86-2	97.5 (89.0)[b]
1b	$PhCH_2CH_2COCl$	645-45-4	Me_4Sn		$PhCH_2CH_2COMe$	2550-26-7	99.5
1c		17082-09-6	Me_4Sn			1896-62-4	91.3[b]
1d		527-69-5	Me_4Sn			1192-62-7	91.0
1e	CH_3COCl	75-36-5	Ph_4Sn		$PhCOMe$		76.3
1f	$(CH_3)_3CCOCl$	3282-30-2	Me_4Sn		$(CH_3)_3CCOMe$	75-97-8	82.2
1g	$CH_2{=}CHCOCl$	814-68-6	Me_4Sn		$CH_2{=}CHCOMe$	78-94-4	93.3
1h	$ClCO(CH_2)_4COCl$	111-50-2	Me_4Sn		$MeOC(CH_2)_3COMe$	13505-34-5	90.5[b]
1i		54941-52-5	Me_4Sn			69461-74-1	88.0[b]
1j	$ClCOCOCl$	79-37-8	Me_4Sn		$MeCOMe$	67-64-1	10.0
2a	$4\text{-}CH_3OC_6H_4COCl$	100-07-2	Ph_4Sn	595-90-4	$4\text{-}CH_3OC_6H_4COPh$	611-94-9	84.7
2b	$4\text{-}CNC_6H_4COCl$	6068-72-0	Me_4Sn		$4\text{-}CNC_6H_4COMe$	1443-80-7	99.8
2c	$4\text{-}ClC_6H_4COCl$	122-01-0	Me_4Sn		$4\text{-}ClC_6H_4COMe$	99-91-2	97.6
2d	$4\text{-}BrC_6H_4COCl$	586-75-4	Me_4Sn		$4\text{-}BrC_6H_4COMe$	99-90-1	67.5
					$4\text{-}MeC_6H_4COMe$	122-00-9	25.9
2e	$4\text{-}NO_2C_6H_4COCl$	122-04-3	Me_4Sn		$4\text{-}NO_2C_6H_4COMe$	100-19-6	98.7
2f	$2\text{-}NO_2C_6H_4COCl$	610-14-0	Me_4Sn		$2\text{-}NO_2C_6N_4COMe$	577-59-3	73.3
2g	$4\text{-}CHOC_6H_4COCl$	16173-52-7	Me_4Sn		$4\text{-}CHOC_6H_4COMe$	3457-45-2	86.0[b]
2h	$2\text{-}CH_3COOC_6H_4CO\text{-}Cl$	5538-51-2	Me_4Sn		$4\text{-}CH_3COOC_6H_4COMe$	13031-43-1	95.5[b]
3a	$PhCOCl$		Ph_4Sn		$PhCOPh$	119-61-9	85.7[b]
3b	$PhCOCl$		Ph_3SnMe	1089-59-4	$PhCOPh$		96.8[c]
3c	$PhCOCl$		$(PhCH_2)_4Sn$	10113-29-8	$PhCH_2COPh$	451-40-1	95.0[b]
3d	$PhCOCl$		Me_3SnCH_2Ph	4314-94-7	$PhCH_2COPh$		91.5
3e	$PhCOCl$		Me_4Sn		$PhCOMe$		97.5
3f	$PhCOCl$		$(n\text{-}Bu)_4Sn$	1461-25-2	$PhCO(n\text{-}Bu)$	1009-14-9	91.3
3g	$MeOCO(CH_2)_3COCl$	1501-26-4	$(n\text{-}Bu)_3Sn\text{-}CH{=}CH_2$	7486-35-3	$MeOCO(CH_2)_3COCH\text{-}{=}CH_2$	34990-33-5	92.5[b]
3h	$PhCOCl$		Me_3SnCl	1066-45-1	$PhCOMe$		90.5
3i	$PhCOCl$		Me_2SnCl_2	753-73-1			no reaction
3j	$PhCOCl$		$MeSnCl_3$	993-16-8			no reaction

[a] By GLC, based on the acid chloride. [b] Isolated yield. [c] No acetophenone was detected.

group. Thus, the reaction of benzoyl chloride with trimethyltin chloride under the conditions of Table I takes five times longer to reach completion than the corresponding reaction utilizing tetramethyltin. Although the symmetrization reaction of the trimethyltin chloride to give tetramethyltin (eq 3) could ac-

$$2Me_3SnCl \rightleftharpoons Me_4Sn + Me_2SnCl_2 \quad (3)$$

count for part of the methyl transfer, by no means can it be responsible for all of the methyl transfer since a quantitative yield of acetophenone is obtained when benzoyl chloride reacts with an equivalent amount of trimethyltin chloride (entry 3h). Since dimethyltin dichloride and methyltin trichloride are unreactive (entries 3i and 3j), they probably do not undergo symmetrization under the reaction conditions.

The order of group transfer from unsymmetrical tetraorganotin does not follow the order of the bond dissociation energies of the tin–carbon bonds. Bond dissociation energies for tin–alkyl groups are smaller than for tin–phenyl or tin–vinyl groups,[8] whereas triphenylmethyltin and tributylvinyltin transfer exclusively the phenyl and vinyl groups, respectively (entries 3b and 3g). This phenomenon is in agreement with the observation that platinum complexes undergo vinylation with no methylation by trimethylvinyltin.[9] Also, although the bond dissociation energies for tin–vinyl and tin–phenyl groups are about the same,[8] transfer of the vinyl group proceeds at a much faster rate. There is a correlation, however, between the tin–carbon bond polarity and the ease of the organic group transfer. The moment of the tin–phenyl group is about twice that of tin–methyl,[8] and the large tin–chlorine bond moment seems to decrease the reactivity of the tin–methyl bonds in trimethyltin chloride considerably by decreasing their effective polarity. Group transfer, therefore, probably is a result of electrophilic attack on the carbon attached to tin. In fact, the above sequence is in agreement with the general sequence observed for electrophilic carbon–tin cleavages.[10] Tetrakis(triphenylphosphine)palladium(0) also catalyzes the reaction; however, it is less effective owing to the triphenylphosphine the complex liberates. Triphenylphosphine has a deactivation effect on the reaction (vide supra). In addition, this complex is air-sensitive and therefore less convenient to handle. Hexamethylphosphoric triamide (HMPA) is the most effective solvent for the reaction although THF can be used also. The reaction of benzoyl chloride and tetramethyltin catalyzed by 1 in THF under the usual reaction conditions gives a 90.5% yield of acetophenone after 21 h, whereas a similar reaction using HMPA as a solvent reaches completion after 10 min. Other polar solvents, e.g., dimethylformamide, *N*-methylpyrrolidone, and tetramethylurea, are even less effective than THF.

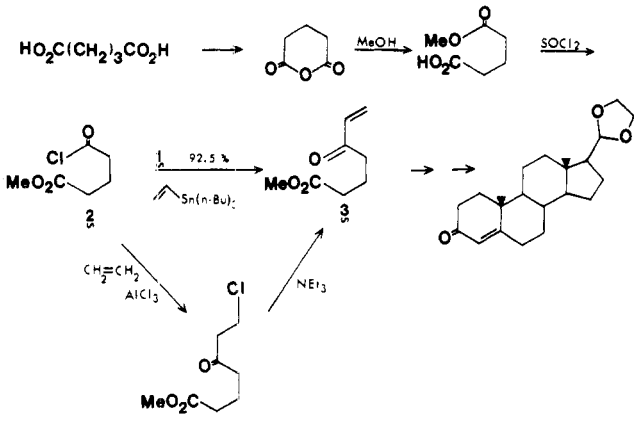
One of the useful applications of this method, for example, is the synthesis of methyl 5-oxo-6-heptenoate (**3**), a key intermediate in a steroid synthesis[11] (Scheme I). The pure

Table II. Dependence of Reaction 4 on Catalyst Concentration[a]

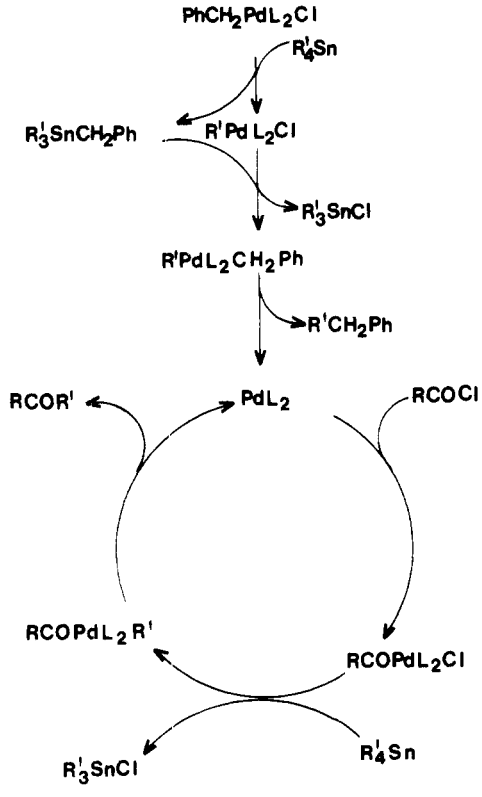
[cat], mol L^{-1} ($\times 10^{-4}$)	turnover no.	initial rate, mol L^{-1} min^{-1} ($\times 10^{-4}$)	$t_{1/2}$, min
0.866	14 925	30.72	125
1.73	7692	76.80	60
6.94	1852	172.80	38
8.30	1563	70.40	50
30.4	422	46.08	128
75.5	170	40.96	115
149.4	86	42.24	120

[a] [PhCOCl] = 1.28 M, [Me_4Sn] = 1.40 M.

Scheme I



Scheme II



product **3** is prepared from **2** in 92.5% yield, whereas the two-step synthesis of **3** from **2**[11] yields, after distillation, only 40–44% of the product contaminated by a considerable amount of dimethyl glutarate. The overall yield of **3** from glutaric acid by the tetramethyltin procedure is 66.3%.

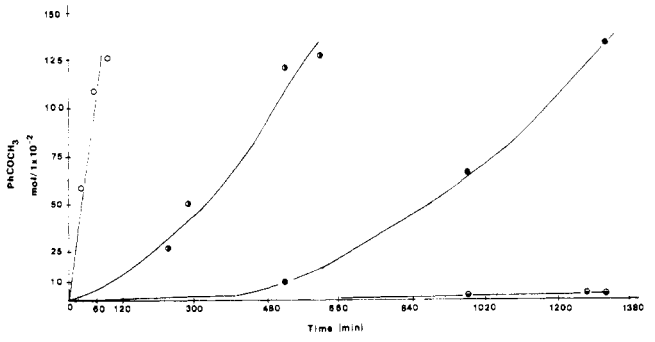


Figure 1. Effect of added triphenylphosphine on reaction 4: [PPh_3] = no PPh_3 (○), 5.12×10^{-3} M (◑), 11.00×10^{-3} M (●), and 34.86×10^{-3} M (◒). Reaction conditions: [PhCOCl] = 1.28 M and [Me_4Sn] = 1.40 M in HMPA at 54 °C under an air atmosphere.

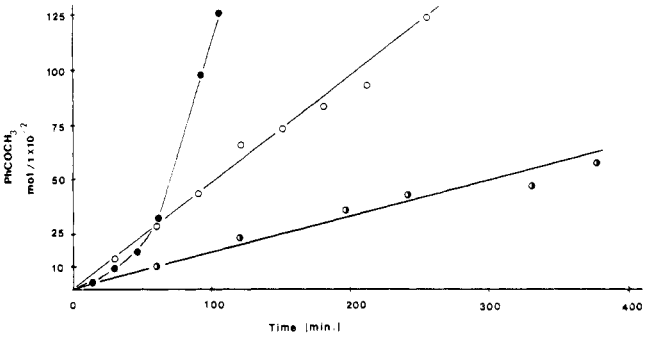
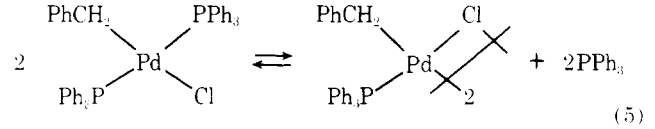


Figure 2. Effect of oxygen on reaction 4: (●) O_2, (○) air, and (◑) argon. Reaction conditions: [cat[1]] = 7.56×10^{-3} M, $[PhCOCl]_0$ = 1.28 M, and [Me_4Sn] = 1.40 M in HMPA at 53 °C.

The catalyst concentration, added triphenylphosphine, and oxygen affect the rate of the reaction of benzoyl chloride with tetramethyltin (eq 4). Very high turnover numbers can be

$$PhCOCl + Me_4Sn \xrightarrow[HMPA]{1} PhCOCH_3 + Me_3SnCl \quad (4)$$

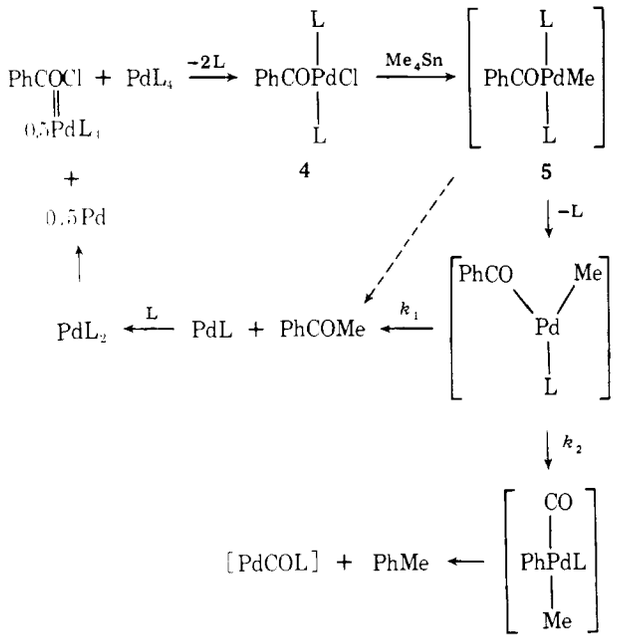
obtained, with the catalyst remaining active as long as the acid chloride is present (Table II). The initial reaction rate and $t_{1/2}$ are very sensitive to catalyst concentration in the range of 0 to 3×10^{-3} M and reach a maximum at about 7×10^{-4} M, whereas the rate and $t_{1/2}$ become constant at catalyst concentrations above 3×10^{-3} M. This behavior is not fully understood. However, deactivation at high catalyst concentrations can be due to dimerization of the catalyst, which liberates triphenylphosphine[12] (eq 5). Triphenylphosphine deac-



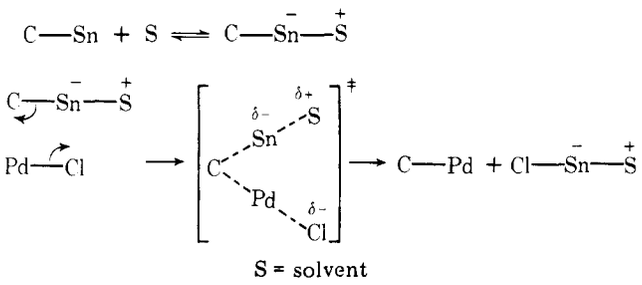
(5)

tivates the reaction (Figure 1) and oxygen has a considerable activation effect (Figure 2), thus making an inert atmosphere disadvantageous. For even faster reactions a pure oxygen atmosphere can be employed, except when oxygen-sensitive compounds, e.g., *p*-formylbenzoyl chloride, are reactants or products. The most plausible mechanism for the reaction is shown in Scheme II. The active catalyst, bis(triphenylphosphine)palladium(0), is generated from **1** by a sequence of double metathesis and reductive elimination, the first being replacement of the benzyl group rather than the chloride.[13] Acid chloride oxidatively adds to the bis(triphenylphosphine)palladium(0), generating the palladium(II) complex which undergoes metathesis with the tin compound and reductively eliminates the product ketone. Analogous mechanistic steps have been proposed for coupling reactions of or-

Scheme III



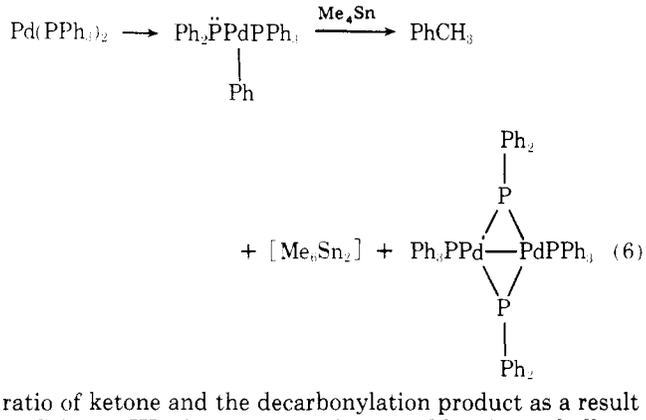
Scheme IV



S = solvent

ganometallic reagents with organic halides catalyzed by palladium and nickel.[14] The product of oxidative addition of benzoyl chloride to tetrakis(triphenylphosphine)palladium(0), *trans*-chloro(benzoyl)bis(triphenylphosphine)palladium(II), reacts stoichiometrically with tetramethyltin to afford acetophenone together with small amounts of toluene, probably as a result of aryl migration in the benzoyl complex (Scheme III).

Toluene also could have been formed as a result of intramolecular oxidative addition of one of the triphenylphosphine ligands to the coordinatively unsaturated bis(triphenylphosphine)palladium(0),[15] followed by metathesis and reductive elimination (eq 6). Thus, in order to determine the



(6)

ratio of ketone and the decarbonylation product as a result of Scheme III, the reaction of *trans*-chloro(4-methylbenzoyl)bis(triphenylphosphine)palladium(II) with tetramethyltin was carried out to yield 78.3% *p*-methylacetophenone, 10.9% *p*-xylene, 25.5% toluene, and 19.2% benzene, based on palladium. Thus, $k_1/k_2 \sim 7$, the ligands being the source of toluene and benzene.

When **4** was allowed to react with tetramethyltin in the presence of added triphenylphosphine, the rate of the reaction was retarded, supporting a mechanism in which triphenylphosphine is dissociated from **5** before the reductive elimination takes place. Such a dissociation of the square-planar trans complex (**5**) puts the groups undergoing reductive elimination in adjacent positions. However, the effect of triphenylphosphine is much smaller than that observed for the catalytic reaction (Figure 1), suggesting that the oxidative addition step is probably that affected to the greatest extent by added triphenylphosphine. Retardation of the oxidative addition reaction by added ligand is well documented.[16] Upon addition of triphenylphosphine to a mixture of **4** and tetramethyltin, a quantitative conversion to acetophenone and tetrakis(triphenylphosphine)palladium(0) takes place, with not even traces of toluene being formed (eq 7). The aryl migration process (Scheme III), which requires a vacant coordination site, apparently is much more sensitive to added ligand than the reductive elimination. In theory, reductive elimination can take place without prior phosphine dissociation by conversion of the square-planar **5** into a transient tetrahedral complex, putting the eliminating groups in adjacent positions. An associative mechanism probably does not operate since triphenylphosphine retards the reactions.

$$PhCOPd(PPh_3)_2Cl + Me_4Sn \xrightarrow{PPh_3} PhCOMe + Pd(PPh_3)_4 + Me_3SnCl \quad (7)$$

Oxygen has a slight retarding effect on the reaction of **4** and tetramethyltin in contrast to the marked accelerating effect it has on the catalytic reaction. Thus, it is most likely the oxidative addition reaction which is accelerated by oxygen. The considerable influence of the oxidative addition step on the overall reaction points out that this step is slow and could be rate determining. The marked influence that triphenylphosphine has on the catalytic reaction compared with the small effect it has on the reaction of **4** with tetramethyltin also can be rationalized on this basis. Zinc chloride has no accelerating effect on the reaction of **4** and tetramethyltin or on reaction 4. Since zinc chloride has been shown[17] to enhance the transmetalation rate between zirconium and aluminum compounds to nickel or palladium complexes, it could be assumed that the transmetalation steps involved in reaction 4 are fast. The sequence of the organic group transfer from unsymmetrical tetraorganotins, which is the same as for electrophilic carbon–tin cleavages (vide supra), points out that the transmetalation reaction between **4** and the tetraorganotin is probably an electrophilic attack on the carbon attached to tin by the electron deficient Pd(II). Polar solvents are known to play an important role in electrophilic cleavages of carbon–tin bonds.[10] Such solvents form a "collision complex" whose carbon atoms are susceptible to attack by electrophiles, yielding an open transition state, the existence of which has been reasonably well established[18] (Scheme IV). The nucleophilicity of the solvent toward tin (which seems to be the most important factor affecting the polarity of the solvents for electrophilic substitution)[19] was found to be the largest for HMPA.[20]

In view of this proposed mechanism, it was assumed that carbonylation of organic halides to ketones could be effected (eq 8). Oxidative additions of alkyl and aryl halides to palladium(0) complexes as well as carbonylation of palladium–carbon σ bonds are well-known processes.[21] However, at-

$$RX + R'_4Sn + CO \xrightarrow{1} RCOR' + R'_3SnX \quad (8)$$

tempts to carbonylate bromobenzene gave only 1.4% acetophenone, and *m*-nitrobromobenzene, which undergoes faster oxidative addition to Pd(0), yielded only 2.1% *m*-nitroacetophenone. Dissappointing results were obtained when benzyl chloride was used.

Experimental Section

All melting points are uncorrected. ^{1}H NMR spectra were obtained on JEOL MH-100 or Varian EM-360 spectrophotometers with Me_4Si as an internal standard in $CDCl_3$ as solvent. GLC analyses were performed on a Varian Aerograph 700 using a 0.25 in. × 6 ft column packed with 20% Carbowax 20M on Chromosorb W. IR spectra were obtained on a Beckman Acculab 3.

Acid chlorides or the corresponding carboxylic acids were obtained commercially and used as received, except for benzoyl chloride which was distilled prior to its use in the kinetic experiments. Tetramethyltin, tetrabutyltin, tetraphenyltin, tetravinyltin, trimethyltin chloride, dimethyltin dichloride, methyltin trichloride, and triphenylmethyltin were obtained commercially and used without further purification. Tetrabenzyltin,[22] tributylvinyltin,[23] tetrakis(triphenylphosphine)palladium(0),[24] benzylchlorobis(triphenylphosphine)palladium(II),[12] and benzoylchlorobis(triphenylphosphine)palladium(II)[25] were prepared according to published procedures. HMPA was dried over 4 Å molecular sieves; THF was dried over sodium and distilled before use.

General Procedure for Ketone Preparation. To a solution of 36.0 mmol of the acid chloride in 16 mL of HMPA was added 36.4 mmol of the tin compound and 1.8×10^{-2} mmol of **1** (except when tetraphenyltin was used, in which case a suspension of 14.8 mmol of tetraphenyltin in 60 mL of HMPA was used, together with 14.8 mmol of the acid chloride and 0.16 mmol of **1**). The yellow solution was heated at 65 °C with stirring under an air atmosphere in a sealed tube until blackening occured (1 min to hours). The solution was cooled to room temperature, and 5 mL of water was added. The mixture was extracted with 3 × 10 mL of ether (when the product ketone was soluble in hexane, this solvent, in which HMPA has a low solubility, was used). The etheral solutions were combined and washed with 2 × 10 mL of water and dried over $MgSO_4$, and the solvent was removed by evaporation. The residue was purified by distillation or crystallization.

Methylglutaryl Chloride. Glutaric anhydride, formed from glutaric acid (100 g) and acetic anhydride, was used without purification for the preparation of methyl hydrogen glutarate[26] (91 g, 82.9%): NMR δ 1 80–2.65 (m, 6 H), 3.70 (s, 3 H), 11.50 (s, 1 H). This acid ester was converted into the corresponding acid chloride with thionyl chloride (89.3 g, 87.1%): bp 74–75 °C (4 mmHg) [lit.[26] 98 °C (10 mmHg)]; NMR δ 1.80–2.60 (m, 4 H), 3.00 (t, J = 7 Hz, 2 H), 3.66 (s, 3 H).

Methyl 5-Oxo-6-heptenoate. Tributylvinyltin (4.0 g., 12.63 mmol) and 41.6 mg (5.50×10^{-2} mmol) of **1** were added to a solution of 2.00 g (12.16 mmol) of methylglutaryl chloride in 8 mL of HMPA. The clear yellow solution was heated at 65 °C with stirring under an air atmosphere, and after 1 min an instantaneous color change to black occurred. The solution was cooled to room temperature, and 40 mL of water was added. NaCl (~1 g) was added to the mixture, and it was extracted with 4 × 60 mL of ether. The ether extracts were combined, washed with 4 × 50 mL of water, and dried over $MgSO_4$. The solvent was removed by evaporation. The ^{1}H NMR spectrum of the residue indicated that it was a mixture of the desired product and Bu_3SnCl. The residue was redissolved in ether, and 20 mL of a half-saturated alcoholic solution of KF was added. The white percipitate of Bu_3SnF formed immediately and was filtered. The solvent was removed by evaporation, and the residue was purified by distillation to afford 1.75 g (92.5%) of methyl 5-oxo-6-heptenoate: bp 104–106 °C (15 mmHg) [lit.[11] 69–85 °C (1.5 mmHg)]; NMR δ 1.80–2.85 (m, 6 H), 3.65 (s, 3 H), 5.70–6.35 (m, 3 H).

***p*-Acetylbenzaldehyde.** To a solution of 16.1 mg (0.021 mmol) of **1** in 4 mL of HMPA was added 1.106 g (6.56 mmol) of *p*-formylbenzoyl chloride. The solution was degassed, and the flask was filled with argon (to prevent oxidation of the aldehyde). To this mixture was added 7.2 mL (8.65 mmol) of Me_4Sn via a syringe, and the clear yellow solution was stirred at 65 °C for 25 h. Although there was no color change after this period, the reaction was stopped to avoid Pd metal catalyzed decarbonylation of the aldehyde. After the mixture was cooled to room temperature, 5 mL of water was added and the mixture was extracted with 5 × 30 mL of pentane. The pentane extracts were combined, dried over $MgSO_4$, concentrated to a volume of 15 mL, and kept at −15 °C overnight. The white needles of the product were collected by filtration and vacuum-dried, yielding 835 mg (86.0%) of *p*-acetylbenzaldehyde: mp 33–34 °C (lit.[7] 32.9–34 °C); IR (neat) $\nu_{C=O}$ 1695, 1715 cm^{-1}; NMR δ 2.60 (s, 3 H), 7.96 (q, A_2B_2, 4 H), 10.05 (s, 1 H).

***o*-Hydroxyacetophenone Acetate.** This compound was prepared from acetylsalicyloyl chloride and tetramethyltin according to the general procedure. Blackening took place after 30 min, and the crystalline product was isolated in 95.5% yield: mp 85–86 °C (lit.[27]); NMR δ 2.30 (s, 3 H), 2.58 (s, 3 H), 7.00–7.95 (m, 4 H).

2,7-Octanedione. This compound was prepared from 627 mg (3.43 mmol) of adipoyl chloride and 1.10 mL (7.94 mmol) of tetramethyltin in 90.5% yield: NMR δ 1.3–3.0 (m), 2.10 (strong singlet in middle of multiplet). The oily product was converted into the dioxime by refluxing its ethanolic solution with hydroxylamine hydrochloride and pyridine for 5 h. The dioxime was recrystallized from ethanol, mp 157–158 °C (lit.[28] 158 °C).

***trans*-4-Phenyl-3-buten-2-one.** This ketone was prepared in 91.3% yield from *trans*-cinnamoyl chloride and tetramethyltin according to the general procedure and crystallized from hexane: mp 39–40 °C (lit.[28] 40–42 °C); ^{1}H NMR δ 2.35 (s, 3 H), 6.70 (d, J = 16 Hz, 1 H), 2.37 (m, 6 H). Tetramethyltin or trimethyltin chloride does not undergo conjugate addition to the product α,β-unsaturated ketone under the reaction conditions as shown by another experiment in which a solution of 1.106 g (7.56 mmol) of *trans*-4-phenyl-3-buten-2-one, 1.10 mL (7.92 mmol) of tetramethyltin, 1.514 g (7.600 mmol) of trimethyltin chloride, and 17.7 mg (0.023 mmol) of **1** in 4 mL of HMPA was heated at 65 °C with stirring for 18 h. GLC analysis (155 °C, 20% DEGS on Chromosorb W) using benzophenone as an internal standard showed that the starting unsaturated ketone remained unchanged.

Benzyltrimethyltin. This compound was prepared by analogy to the preparation of phenyltrimethyltin[29] in 73% yield: bp 88–91 °C (9 mmHg) [lit.[30] 90 °C (8 mmHg)]; NMR δ 0.03 (s, 9 H), 2.30 (s, 2 H), 6.9–7.5 (m, 5 H); $J(^{117}Sn-CH_3)$ = 25 Hz, $J(^{119}Sn-CH_3)$ = 26 Hz, $J(^{117}Sn-CH_2Ph)$ = 30 Hz.

Chloro(4-methylbenzoyl)bis(triphenylphosphine)palladium(II). A suspension of 1.584 g (1.372 mmol) of tetrakis(triphenylphosphine)palladium(0) and 1.00 mL (7.56 mmol) of freshly distilled *p*-toluoyl chloride in 120 mL of degassed anhydrous benzene was stirred at room temperature under nitrogen. Within 5 min all of the solid dissolved and stirring was continued for 16 h. The solution was concentrated to a volume of ~20 mL, and the complex was precipitated by addition of 1:1 hexane–ether. The mixture was cooled at 0 °C for 7 h, and the lemon-yellow chloro(4-methylbenzoyl)bis(triphenylphosphine)palladium(II) was isolated by filtration, washed with ether, and vacuum-dried to give 950 mg (88.2%): mp 143–145 °C dec; NMR δ 2.15 (s, 3 H), 6.65 (q, A_2B_2, 4 H), 6.85–7.80 (m, 30 H). Anal. Calcd for $C_{44}H_{37}ClOP_2Pd$: C, 67.27; H, 4.71; Cl, 4.52; P, 7.89. Found: C, 67.53; H, 4.76; Cl, 4.60; P, 7.77.

Reaction of Chlorobenzoylbis(triphenylphosphine)palladium(II) with Tetramethyltin. (a) In the Presence of Added Triphenylphosphine. A suspension of 327.2 mg (0.42 mmol) of chlorobenzoylbis(triphenylphosphine)palladium(II) and 222.6 mg (0.850 mmol) of triphenylphosphine in 1.5 mL of HMPA was degassed, and 0.500 mL (3.61 mmol) of Me_4Sn was added via a syringe. The yellow suspension was heated at 64 °C with stirring under nitrogen for 5 h and cooled at 0 °C overnight. The yellow air-sensitive tetrakis(triphenylphosphine)palladium(0) was isolated by filtration under nitrogen, washed with degassed ether, and vacuum-dried to give 414.5 mg (84.7%) of product, mp 113–116 °C (lit.[24] 116 °C). The IR spectrum was superimposable on that of an authentic sample of tetrakis(triphenylphosphine)palladium(0).

The filtrate and ethereal washings were combined, and 100 μL of *p*-methylacetophenone was added as an internal standard. GLC analysis of the solution (220 °C, 10 ft × 0.325 in., 20% Carbowax 20M on Chromosorb W 60/80) showed a 100% yield of acetophenone. The ketone was isolated by preparative GLC, and its identity was confirmed by NMR: δ 1.9 (s, 3 H), 7.2 (m, 5 H).

(b) In the Absence of Added Triphenylphosphine. The reaction was repeated except that triphenylphosphine was not added. The mixture blackened after 5 min at 65 °C, and heating was continued for 7 h. *p*-Methylacetophenone and *sec*-butylbenzene were added as internal standards, followed by 5 mL of water. GLC analysis of the combined ethereal extracts of the mixture showed 73.4% acetophenone in addition to 34.6% toluene and 17.4% benzene.

(c) At Room Temperature under an Air Atmosphere. A yellow suspension of 350.3 mg (0.454 mmol) of chlorobenzoylbis(triphenylphosphine)palladium(II) and 120 μL (0.867 mmol) of tetramethyltin in 5 mL of HMPA stirred at room temperature blackened after 3.5 h. The usual workup and GLC analysis showed the formation of 73.3%

acetophenone, 21.8% toluene, and 1.8% benzene. Essentially the same results were obtained when the reaction was performed in the presence of 0.944 mmol of *p*-chlorobenzoyl chloride.

(d) Effect of Oxygen, Triphenylphosphine, *m*-Dinitrobenzene, and $ZnCl_2$. A suspension of 308 mg (0.399 mmol) of chlorobenzoylbis(triphenylphosphine)palladium(II) and 150 μL (1.084 mmol) of tetramethyltin in 4.3 mL of HMPA was stirred at 28 °C for 130 min (1) under argon, (2) under oxygen, (3) in the presence of 205.8 mg (1.225 mmol) of *m*-dinitrobenzene, (4) in the presence of 250.9 mg (0.958 mmol) of triphenylphosphine, and (5) in the presence of 50 mg of $ZnCl_2$. The usual workup and GLC analysis showed that the following yields of acetophenone were obtained, respectively: (1) 74.2, (2) 47.2, (3) 52.7, (4) 21.2, (5) 41.4%.

Reaction of Chloro(4-methylbenzoyl)palladium(II) with Tetramethyltin. A suspension of 272.9 mg (0.350 mmol) of chloro(4-methylbenzoyl)palladium(II) and 0.500 mL (3.61 mmol) of tetramethyltin was stirred at room temperature for 7 h, after which time the mixture blackened. Acetophenone and *sec*-butylbenzene were added as internal standards, and GLC analysis (120–190 °C, 20% Carbowax 20M) after the usual workup showed the formation of the following products: *p*-methylacetophenone (78.3%), *p*-xylene (10.9%), toluene (25.5%), benzene (19.2%).

Kinetic Experiments. The kinetic experiments were conducted in Schlenk tubes equipped with rubber septums and immersed in a constant temperature oil bath. Freshly distilled benzoyl chloride was used, and *p*-methylacetophenone served as an internal standard. At certain intervals small samples of the solutions were withdrawn via a syringe and were quenched by injection into hexane-filled vials. The complex precipitated immediately, and the hexane solution was analyzed by GLC.

Attempted Ketone Synthesis by Carbonylation. To a solution of 1.193 g (7.60 mmol) of bromobenzene and 73.4 mg (0.097 mmol) of I in 4 mL of HMPA in a 90-mL pressure tube was added 2.00 mL (14.44 mmol) of tetramethyltin. The solution was pressurized with 30 atm of CO (in addition to 1 atm of air present) and heated at 65 °C with stirring for 15 h, during which time the Pd metal precipitated and the CO pressure dropped to 2.5 atm (at room temperature). The usual workup of the reaction mixture and GLC analysis showed that only 1.4% of acetophenone was formed (111.7% based on the catalyst), with 95.7% of the bromobenzene remaining unchanged. Similar results were obtained when tetrakis(triphenylphosphine)palladium(0) was used as catalyst. When *m*-nitrobromobenzene was allowed to react with tetramethyltin using this catalyst, 2.4% of *m*-nitroacetophenone was obtained, and 4.1% of this product was formed when the CO pressure was lowered to 1.1 atm.

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Registry No.—1, 22784-59-4; glutaric anhydride, 108-55-4; methyl hydrogen glutarate, 1501-27-5; chloro(4-methylbenzoyl)bis(triphenylphosphine)palladium(II), 69469-77-8; tetrakis(triphenylphosphine)palladium(0), 14221-01-3.

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Synthesis of New Branched-Chain Cyclitols Having Epi and Allo Configuration and Myo Configuration Respectively from 3-*O*-Benzyl-5,6-dideoxy-5-[*C*-(1,3-dithian-2-yl)]-6-nitro-D-allofuranose and -L-talofuranose[1a]

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The Michael addition of 2-lithio-1,3-dithiane to 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-α-D-*ribo*-hex-5-enofuranose (**3**) gave 3-*O*-benzyl-5,6-dideoxy-5-*C*-(1,3-dithian-2-yl)-1,2-*O*-isopropylidene-6-nitro-β-L-talofuranose (**4**) and -α-D-allofuranose (**5**) in 59% yield (**4**:**5** = 1:1). Intramolecular cyclization of these compounds in weak basic conditions after removal of the isopropylidene group gave branched-chain cyclitols having epi and allo configuration (**11** and **15**) from **5** and myo configuration (**7**) from **4**, respectively, in good yields, and the stereochemistry of cyclization was discussed. The cyclization of 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-(nitromethyl)-6-nitro-α-D-*ribo*-hexofuranose prepared by the addition of nitromethane to **3** was also described.

In a previous paper,[1b] we reported a simple stereoselective synthesis of branched-chain cyclitols having myo and muco configuration by an intramolecular cyclization of 3-*O*-benzyl-5,6-dideoxy-5-*C*-(1,3-dithian-2-yl)-6-nitro-D-glucofuranose and -L-idofuranose, respectively, in weak basic conditions. In that paper, we disclosed that two bulky groups such as benzyloxy at C-3 and 1,3-dithiane residue at C-5

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