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Registry No. 1, 63160-46-3; 2, 73151-59-4; 3, 63160-44-1; 5, 33524-31-1; 6, 71255-06-6; 7, 71255-03-3; 8, 71255-05-5; 9, 70738-04-4; 10, 70738-05-5; 11, 56964-06-8; 12, 81477-60-3; 13, 81477-61-4; 14, 81477-62-5; 15, 81477-63-6; 15a, 81477-64-7; 16, 81477-65-8; 17, 81477-66-9; 18, 81477-67-0; *trans*-20, 81477-68-1; *cis*-20, 81477-69-2; 21, 81477-70-5; 22, 81477-71-6; 23, 81477-72-7; 24, 18409-21-7; 25, 63127-63-9; 26, 81477-73-8; 4-iodo-3,6-dimethoxybenzyl alcohol, 81477-74-9; 1-chloro-1-decen-3-one, 18201-31-5; octanoyl chloride, 111-64-8; 1-iodo-1-decen-3-one, 81477-75-0; 1-iodo-1,3-decadiene, 81477-76-1; 1-iodo-3-bromo-1-decene, 81477-77-2.

Palladium-Catalyzed Reactions of Acyl Chlorides with (1-Alkynyl)tributylstannanes. A Convenient Synthesis for 1-Alkynyl Ketones

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Acyl chlorides couple with (1-alkynyl)tributylstannanes in the presence of catalytic amounts of palladium(II) or palladium(0) complexes to produce 1-alkynyl ketones in respectable yields. The couplings of isobutyryl, acetyl, benzoyl, and *p*-nitrobenzoyl chlorides with phenylethynyl-, (trimethylsilyl)ethynyl-, (carbomethoxy)ethynyl-, [3-[(*tert*-butyldimethylsilyl)oxy]-1-propynyl]-, and (3,3-diethoxy-1-propynyl)tributylstannanes were investigated in the presence of tetrakis(triphenylphosphine)palladium(0), benzylchlorobis(triphenylphosphine)palladium(II), dichlorobis(triphenylphosphine)palladium(II), or phenyliodobis(triphenylphosphine)palladium(II). The reactions are highly selective in that only the alkynyl groups are transferred from the stannane.

As a class, α,β-acetylenic carbonyl compounds are extremely versatile substrates for further synthetic elaboration. Numerous syntheses involving α,β-acetylenic carbonyl compounds have been reported,[2] and a significant number of them involve the synthesis of heterocyclic compounds. The facility with which α,β-acetylenic carbonyl compounds undergo nucleophilic additions and cyclizations[2c,d,3-6] makes them very desirable intermediates for elaboration to heterocyclic systems. Our interest in this class of compounds derives from their use as intermediates for *C*-nucleoside synthesis.[3-5] More specifically, we are interested in developing convenient, high-yield routes for converting carboxylic acids into 1-alkynyl ketones, which could serve as precursors to *C*-nucleosides.

A survey of the literature revealed the existence of several methods for carrying out such transformations; however, there are limitations with each of them. (1) The silver or copper(I) acetylide–acyl chloride routes[7-9] are quite variable in yield, and acetal or ester functions in the acetylide are often cleaved by the acyl chloride.[10] (2) The $AlCl_3$-catalyzed reaction of acyl chlorides with silylated alkynes[11] uses strongly acidic conditions. (3) The use of alkynylcadmium–acyl chloride[12] and of alkynyllithium–mixed anhydride[13] procedures gives low to moderate yields of 1-alkynyl ketones, and they place limitations on the functionalities allowed in the acetylene. (4) The copper(I) iodide–dichlorobis(triphenylphosphine)palladium(II)-catalyzed reaction of acyl chlorides with 1-alkynes[14] cannot be used with acyl chlorides that readily react with tertiary amines, which are necessary components of the reaction. (5) Thermal reactions between acyl chlorides and stannylated alkynes[15] give only moderate yields of 1-alkynyl ketones.

Since the above syntheses either give low yields of 1-alkynyl ketones or are of limited scope, we looked for a route to 1-alkynyl ketones that would be clean, produce high yields, and tolerate a wide variety of functional groups on both reactants. Most recently, the conversion of acyl chlorides into ketones by a palladium-catalyzed reaction with tetraorganotin reagents (eq 1) was reported.[16] The

$$R'_4Sn + RC(O)Cl \xrightarrow{\text{Pd catal}} RC(O)R' + R_3'SnCl \quad (1)$$

reaction is mild, tolerates a variety of functional groups, and produces ketones in high (usually >90%) yield. Furthermore, when vinyl- or aryltrialkylstannanes were used, only the vinyl or aryl group was transferred to form the corresponding ketones. We reasoned that an alkynyl

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group might also be selectively transferred from an alkylnylstannane, thus providing a new, mild, and high-yield route to 1-alkynyl ketones.

We now report the synthesis of a variety of (1-alkynyl)tributylstannanes and their reactions with acyl chlorides to produce 1-alkynyl ketones in the presence of the palladium catalysts benzylchlorobis(triphenylphosphine)palladium(II) (**1**), dichlorobis(triphenylphosphine)palladium(II) (**2**), tetrakis(triphenylphosphine)palladium(0) (**3**), and phenyliodobis(triphenylphosphine)palladium(II) (**4**).

Initially, we examined the reaction between (phenylethynyl)tributylstannane (**5a**), prepared by the action of phenylethynyllithium on chlorotributylstannane, and isobutyryl chloride in the presence of catalyst **1** (eq 2) to

$$\underset{\textbf{5a-e}}{RC(O)Cl} + Bu_3SnC{\equiv}CR' \xrightarrow{2} \underset{\textbf{6-19}}{RC(O)C{\equiv}CR'} + Bu_3SnCl \quad (2)$$

5a, R′ = Ph
b, R′ = $(EtO)_2CH$
c, R′ = Me_3Si
d, R′ = *t*-$BuMe_2SiOCH_2$
e, R′ = MeO_2C
6, R = *i*-Pr; R′ = Ph
7, R = R′ = Ph
8, R = *p*-O_2NPh; R′ = Ph
9, R = Me; R′ = Ph
10, R = *i*-Pr; R′ = $(EtO)_2CH$
11, R = Me; R′ = $(EtO)_2CH$
12, R = Ph; R′ = $(EtO)_2CH$
13, R = *i*-Pr; R′ = Me_3Si
14, R = Ph; R′ = Me_3Si
15, R = *p*-O_2NPh; R′ = Me_3Si
16, R = Me; R′ = *t*-$BuMe_2Si$
17, R = *i*-Pr; R′ = *t*-$BuMe_2SiOCH_2$
18, R = Ph; R′ = *t*-$BuMe_2SiOCH_2$
19, R = *i*-Pr; R′ = MeO_2C

[a] Reactions were run with $1:1:(1.8 \times 10^{-2})$ ratios (millimoles) of RCOCl/stannane/2 in 5 mL of $ClCH_2CH_2Cl$ at 84° for 2 h. [b] Isolated yields after 15 min treatment with aq. KF. These are the highest yields of several runs, but were reproducible within 2–3%. [c] 5 min treatment with aq. KF.

optimize the reaction conditions. Catalyst **1** and hexamethylphosphoramide (HMPA) were chosen as the catalyst/solvent system because it is the most effective combination of those examined to date for alkyl and alkenyl transfer from stannanes.[16] Optimum yields of 1-phenyl-4-methyl-1-pentyn-3-one (**6**) were obtained by heating an HMPA solution of equimolar amounts of stannane **5a** and isobutyryl chloride that was also 3.6×10^{-3} M in catalyst **1** for 16 h at 65 °C. Greater concentrations of **1** were not beneficial, whereas smaller concentrations were detrimental. Although HMPA and **1** were the solvent and catalyst of choice for alkyl and alkenyl transfers, we desired a substitute for HMPA because of its adverse biological effects[17] and its hygroscopic nature, and we compared the effectiveness of **1** to three other palladium catalysts, **2–4**.

We selected 1,2-dichloroethane as a substitute for HMPA since it readily dissolves **1** and has a convenient boiling point, 84 °C. Use of 1,2-dichloroethane required changes in temperature and time, 84 °C and 2 h, to obtain optimum conditions. Entries 1–3 in Table I clearly show that HMPA offers no advantage over 1,2-dichloroethane; in fact, the latter is the solvent of choice because of its nonhygroscopic nature, greater ease of removal, and lack of the adverse biological properties.

A comparison of the effectivenesses of catalysts **1–4** (entries 3–6, Table I) shows little difference in the catalytic effectiveness of **1** and **3**, whereas **2** is somewhat better than both of them. Although there are only small differences among **1–3**, all three are far superior to **4**. Entry 7 in Table I shows that ketone **6** is produced even in the absence of a palladium catalyst, but the yield is very low. To make certain that isobutyryl chloride was not biased toward either **1** or **2**, we conducted another set of reactions between benzoyl chloride and **5a** with **1** and **2** as catalysts (entries 8 and 9, Table I). Here, **1** and **2** were equally effective. Even though there is little difference in effectiveness among **1–3**, **2** is the preferred catalyst because it is the easiest of the three to prepare,[18-20] and it has a far greater shelf life than **1** or **3**. Catalysts **1** and **3** slowly decompose on standing, even at 0 °C, as indicated by their darkening from a light yellow to a dark brown color; however, **2** appears to be stable indefinitely at room temperature.

Once we had settled on the use of catalyst **2**, we investigated the tolerance of various functional groups and the effects of structural changes in the acyl chloride. These investigations were conducted by studying the reactions of isobutyryl, acetyl, benzoyl, and *p*-nitrobenzoyl chlorides with stannane **5a**, (3,3-diethoxy-1-propynyl)tributylstannane (**5b**), [(trimethylsilyl)ethynyl]tributylstannane (**5c**), [3-[(*tert*-butyldimethylsilyl)oxy]-1-propynyl]tributylstannane (**5d**), and [(carbomethoxy)ethynyl]tri-

Table I. Optimization of Formation of Ketone 6 from 5a[a]

entry	R in RCOCl	catalyst	temp, °C	time,[b] h	solvent	yield,[c] %
1	*i*-Pr	1	65	16	B	66
2	*i*-Pr	1	65	16	A	64
3	*i*-Pr	1	84	2	A	69
4	*i*-Pr	2	84	2	A	77
5	*i*-Pr	3	84	2	A	71
6	*i*-Pr	4	84	2	A	29
7	*i*-Pr		84	18	A	15
8	Ph	1	84	2	A	94
9	Ph	2	84	2	A	94

[a] Reactions were run with $1:1:(1.8 \times 10^{-2})$ ratios (millimoles) of RCOCl/**5a**/catalyst in 5 mL of solvent A ($ClCH_2CH_2Cl$) or solvent B (HMPA). [b] Time for optimum yield. [c] Isolated yields after 15 min treatment with aqueous KF. These are the highest yields of several runs but were reproducible within 2–3%.

Table II. Preparation of 1-Alkynyl Ketones from Stannanes 5a-e[a]

entry	R in RCOCl	stannane	ketone (% yield)[b]
1	*p*-O_2NPh	**5a**	**8** (57)
2	Me	**5a**	**9** (55)
3	*i*-Pr	**5b**	**10** (70)
4	Me	**5b**	**11** (31)
5	Ph	**5b**	**12** (68)
6	*i*-Pr	**5c**	**13** (40)
7	*i*-Pr	**5c**	**13** (71)[c]
8	Ph	**5c**	**14** (64)[c]
9	*p*-O_2NPh	**5c**	**15** (51)[c]
10	Me	**5d**	**16** (48)
11	*i*-Pr	**5d**	**17** (60)
12	Ph	**5d**	**18** (66)
13	*i*-Pr	**5e**	**19** (67)

[a] Reactions were run with $1:1:(1.8 \times 10^{-2})$ ratios (millimoles) of RCOCl/stannane/2 in 5 mL of $ClCH_2CH_2Cl$ at 84 ° for 2 h. [b] Isolated yields after 15 min treatment with aq. KF. These are the highest yields of several runs, but were reproducible within 2–3%. [c] 5 min treatment with aq. KF.

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butylstannane (**5e**). The results are tabulated in Table II and show that the reaction is tolerant of nitro, ester, acetal, and trialkylsilyl functions, which are extremely useful functions with regard to heterocyclic ring synthesis.

Except for the reactions of acetyl chloride with **5b** and **5d** (entries 4 and 10, Table II), all other combinations of alkynylstannanes and acyl chlorides that we tried produced 1-alkynyl ketones in greater than 50% yield. In fact, most combinations gave 1-alkynyl ketones in greater than 60% yield. Benzoyl and isobutyryl chlorides always gave higher yields of 1-alkynyl ketones than did *p*-nitrobenzoyl or acetyl chloride. The lower yields for the alkynyl ketones from acetyl and *p*-nitrobenzoyl chlorides and the range of yields among the other alkynyl ketones may not be entirely due to varying abilities of acyl chlorides to couple with alkynylstannanes but may also result from differing propensities of the alkynyl ketones produced to undergo self-reaction under the reaction conditions. This seems reasonable in light of the facts that all of the alkynyl ketones prepared in this study eventually form highly viscous syrups on standing at room temperature, presumably by oligomerization and/or polymerization, and many transition metals catalyze trimerization, oligomerization, and polymerization of acetylenes.[21] To test this hypothesis, we treated ketone **9** with **2** under the reaction conditions for ketone formation in the absence of acyl chloride and in the absence of both acyl chloride and stannane. In the former case only 21% of **9** was recovered, whereas 86% of **9** was recovered in the latter. Thus the lower yields of various alkynyl ketones are in part, if not entirely, due to their further reactions under the reaction conditions.

With the trimethylsilylated stannane **5c**, a modification of the workup procedure was necessary since the normal 15-min treatment of the crude product with aqueous potassium fluoride to remove chlorotributylstannane resulted in partial desilylation of ketones **13–15** to give the corresponding terminal acetylenes. The desilylation can be minimized by cutting the potassium fluoride treatment to 5 min; any further decrease in time resulted in incomplete removal of chlorotributylstannane.

With the exception of **5e**, the stannanes used in this study were prepared in the same manner as for **5a** by the action of the appropriate alkynyllithium on chlorotributylstannane. Stannane **5e** was prepared by heating methyl propiolate with methoxytributylstannane (eq 3).[22]

$$Bu_3SnOMe + HC{\equiv}CCO_2Me \xrightarrow{\text{reflux}} \mathbf{5e} + MeOH \qquad (3)$$

The alkynyllithium method could not be used for **5e** since alkyl lithiopropiolates are stable only below −78 °C,[23] and higher temperatures are necessary for the alkylation of chlorotributylstannane. When the alkynyllithium route is used, excess alkyllithum should be avoided during the preparation of the alkynyllithiums. Any excess of alkyllithium results in the formation of tetraalkylstannanes, which would produce alkyl ketones as contaminants in the 1-alkynyl ketones if they are not removed before reaction with acyl chlorides. The tetraalkylstannanes can be removed by fractional vacuum distillation, but it is tedious and time consuming.

Although the majority of the alkynylstannanes used in this study were prepared by the alkynyllithium method, we now prefer the alkoxystannane route since it avoids the above complications that can arise with the alkynyllithium method and works well with other acetylenes; e.g., phenylacetylene is converted into **5a** in 84% yield by methoxytributylstannane. Furthermore, the procedure is easier than the alkynyllithium method in that simply heating the alkoxystannane with the acetylene under reflux for several hours followed by distillation affords the alkynylstannane in high yield. It is also less expensive since the alkoxytributylstannane can be readily prepared, quantitatively, by heating the very inexpensive hexabutyldistannoxane, bis(tributyltin)oxide, and dialkyl carbonate under reflux for several hours.[24]

We used tributylstannanes in this study instead of trimethylstannanes, which were most often used in the selective alkenyl transfers,[16] because tributylstannanes are much less expensive (730-fold) than the corresponding trimethylstannanes. However, this is not without consequence because a more involved workup procedure is required to remove the generated chlorotributylstannane as compared to chlorotrimethylstannane. Whereas the latter requires only aqueous extraction, the former requires precipitation as fluorotributylstannane.[16,25]

Mechanistic studies on the coupling reaction have not been done, but it seems very likely that the coupling occurs along lines similar to those proposed for palladium-catalyzed coupling of aryl and alkenyl halides with acetylenes[26] and acyl chlorides with tetraorganostannanes.[16]

In summary, the palladium-catalyzed coupling of acyl chlorides with alkynyltributylstannanes provides a convenient and mild method for synthesizing 1-alkynyl ketones that is complementary to or, when sensitive functional groups are present, superior to existing methods.

Experimental Section

Melting points were obtained on a Thomas-Hoover capillary melting point apparatus and are corrected. All boiling points are uncorrected. IR spectra were recorded on a Perkin-Elmer Model 137 spectrophotometer. ^1H NMR spectra were recorded on a Varian EM390 spectrometer with Me_4Si as an internal reference. Mass spectra were recorded on a Varian MAT CH-5 spectrometer (ionization potential 70 eV). Elemental analyses were performed by Galbraith Laboratories, Inc. Column chromatography was performed on E. Merck silica gel 60 (7734). All glassware was dried overnight at 120 °C prior to use. All solvents were removed from the reaction mixtures under reduced pressure on a rotary evaporator. Solvents that were given extra purification before use listed with their method of purification are as follows: dimethylformamide (DMF), distillation under reduced pressure and storage over 4A molecular sieves; benzene, distillation from sodium and storage over 4A molecular sieves; HMPA, distillation from CaH_2 under reduced pressure and storage over 4A molecular sieves; *p*-dioxane, distillation from the sodium ketyl of benzophenone and storage over 4A molecular sieves; THF, distillation from the sodium ketyl of benzophenone just prior to use; 1,2-dichloroethane, distillation from P_2O_5 and storage over 4A molecular sieves; hexane and $CHCl_3$, simple distillation. All other reagents were used as received.

Tetrakis(triphenylphosphine)palladium(0) (3) was prepared as reported[18] in 94% yield.

Benzylchlorobis(triphenylphosphine)palladium(II) (1) was prepared as reported[19] from benzyl chloride and **3**: 88% yield; mp 138–140 °C dec (lit.[19b] mp 147–151 °C dec).

Dichlorobis(triphenylphosphine)palladium(II) (2) was prepared as reported[20] from $PdCl_2$ and Ph_3P in DMF: 96% yield, mp >225 °C.

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Phenyliodobis(triphenylphosphine)palladium(II) (4) was prepared as reported[27] from iodobenzene and **3**: 93% yield; mp 168–169 °C dec (lit.[27] mp 171–186 °C dec).

3,3-Diethoxy-1-propyne (20) was prepared as reported[28] as a colorless liquid, bp 128 °C [lit.[28] bp 38 °C (10 mm)].

3-[(*tert*-Butyldimethylsilyl)oxy]-1-propyne (21) was prepared by a procedure adopted from a previously reported method.[29] A solution of 5.6 g (0.1 mol) of propargyl alcohol, 18.1 g (0.12 mol) of *t*-$BuMe_2SiCl$, and 17.0 g (0.25 mol) of imidazole in 12 mL of DMF was magnetically stirred for 17 h at room temperature under nitrogen. The mixture was then diluted with 80 mL of pentane and washed (3 × 40 mL) with H_2O. The pentane layer was dried over anhydrous $CaSO_4$, and the solvent was removed. Distillation of the residue gave 15.7 g (96%) of **21**: bp 37–39 °C (4.0 mm); IR (CCl_4) 1360, 2021, 3255 cm^{-1}; NMR (CCl_4) δ 0.1 (s, 6, $SiMe_2$), 0.88 (s, 9, *t*-Bu), 2.23 (t, 1, J = 2 Hz, acetylene H), and 4.22 (d, 2, J = 2 Hz, OCH_2); mass spectrum, m/e (relative intensity) 170 (1.05), 155 (1.04), 127 (5.5), 115 (3.78), 113 (87.39), 101 (1.52), 99 (2.05), 83 (100), 75 (20.10), 59 (6.14), 57 (3.54), 56 (1.54), 55 (1.99), 45 (7.73), 43 (6.91).

Methoxytributylstannane was prepared as reported[23] from hexabutyldistannoxane and dimethyl carbonate in quantitative yield; bp 101–102 °C (0.2 mm) [lit.[24] bp 90 °C (0.1 mm)].

General Procedure for Preparation of (1-Alkynyl)tributylstannanes via Alkynyllithiums. A solution of the alkynyllithium in THF was prepared by treating 30 mmol of acetylene in 20 mL of THF for 25 min at 0 °C with 18.75 mL (30 mmol) of 1.6 M butyllithium in hexane. To this solution was added, dropwise, 9.76 g (8.5 mL, 30 mmol) of chlorotributylstannane in 5 mL of THF. The mixture was stirred overnight (16 h) at room temperature. The mixture was then diluted with CH_2Cl_2, washed with H_2O and saturated NaCl solution, and dried over anhydrous $CaSO_4$. The solvent was removed, and the residue was distilled under reduced pressure to give the desired 1-alkynylstannanes.

(Phenylethynyl)tributylstannane (5a) was prepared from phenylacetylene via the alkynyllithium route in 81% yield as a colorless liquid: bp 116–117 °C (0.18 mm) [lit.[30] bp 174 °C (4 mm)]; NMR (CCl_4) δ 0.4–2.3 (m, 27, 3 Bu), 7.08–7.57 (m, 5, Ph).

Compound **5a** was also prepared in 84% yield by heating 0.95 g (3.0 mmol) of methoxytributylstannane with 0.67 g (6.6 mmol) of phenylacetylene at 110 °C for 3 h followed by distillation. This product was identical in all respects with that prepared by the alkynyllithium route.

(3,3-Diethoxy-1-propynyl)tributylstannane (5b) was prepared from **20** in 88% yield as a colorless liquid: bp 115 °C (0.11 mm); NMR (CCl_4) δ 0.46–2.23 (m, 33, 3 Bu and 2 Me), 3.30–3.87 (m, 4, OCH_2), 5.67 (5, 1, $CH(OEt)_2$).

Anal. Calcd for $C_{19}H_{38}O_2Sn$: C, 54.83; H, 8.96; Sn, 28.52. Found: C, 54.77; H, 9.00; Sn, 28.65.

[(Trimethylsilyl)ethynyl]tributylstannane (5c) was prepared from (trimethylsilyl)acetylene in 91% yield as a colorless liquid: bp 89 °C (0.27 mm); NMR (CCl_4) δ 0.14 (s, 9, $SiMe_3$), 0.4–2.3 (m, 27, 3 Bu).

Anal. Calcd for $C_{17}H_{36}SiSn$: C, 52.74; H, 9.31; Sn, 30.69. Found: C, 52.85; H, 9.42; Sn, 30.42.

[3-[(*tert*-butyldimethylsilyl)oxy]-1-propynyl]tributylstannane (5d) was prepared from **21** in 69% yield as a colorless liquid: bp 122 °C (0.1 mm); NMR (CCl_4) δ 0.1 (s, 6, $SiMe_2$), 0.4–2.3 (m, 36, 3 Bu and *t*-Bu), 4.23 (s, 2, OCH_2).

Anal. Calcd for $C_{21}H_{44}OSiSn$: C, 54.94; H, 9.59. Found: C, 54.79, H, 10.04.

[(Carbomethoxy)ethynyl]tributylstannane (5e) was prepared according to a generalized procedure.[22] A mixture of 9.3 g (29 mmol) of methoxytributylstannane and 5.5 g (65 mmol) of methyl propiolate was heated under reflux (110 °C) for 3 h and then distilled to give 9.9 g (92%) of **5e** as a colorless liquid: bp 112 °C (0.15 mm); NMR (CCl_4) δ 0.4–2.23 (m, 27, 3 Bu), 3.69 (s, 3, OMe).

Anal. Calcd for $C_{16}H_{30}O_2Sn$: C, 51.51; H, 8.11; Sn, 31.81. Found: C, 51.62; H, 8.25; Sn, 31.69.

General Procedure for Synthesis of 1-Alkynyl Ketones. In a 25-mL round-bottomed flask equipped with a magnetic stirring bar were placed 1.8×10^{-2} mmol of the palladium catalyst, 1.0 mmol of alkynyltributylstannane, 1.0 mmol of acyl chloride, and 5 mL of solvent. The mixture was then heated for a period of time. The reaction mixture was cooled to room temperature, diluted with 25 mL of ether, and vigorously stirred with 35–50 mL of saturated aqueous KF for 15 min (with silylated compounds, the KF treatment was limited to 5 min). The precipitated Bu_3SnF was removed by filtration, and the organic layer was dried over anhydrous $CaSO_4$. The solvent was then removed, and the residue was chromatographed on a 1.5 × 40 cm column of silica gel. Methods A–F specify the reaction conditions.

Method A: catalyst **2** in $ClCH_2CH_2Cl$ at 84 °C for 2 h. **Method B**: catalyst **1** in $ClCH_2CH_2Cl$ at 84 °C for 2 h. **Method C**: catalyst **2** in HMPA at 65 °C for 16 h. **Method D**: catalyst **1** in HMPA at 65 °C for 16 h. **Method E**: catalyst **3** in $ClCH_2CH_2Cl$ at 84 °C for 2 h. **Method F**: catalyst **4** in $ClCH_2CH_2Cl$ at 84 °C for 2 h.

1-Phenyl-4-methyl-1-pentyn-3-one (6). Method A. The reaction mixture was chromatographed with 2:100 (v/v) ether/hexane to give 134 mg (77%) of **6** as a pale yellow liquid: bp 94 °C (0.12 mm) [lit.[14] bp 130 °C (3 mm)]; IR (CCl_4) 1675, 2190 cm^{-1}; NMR (CCl_4) δ 1.15 (d, 6, J = 7.5 Hz, 2-Me), 2.69 (septet, 1, J = 7.5 Hz, $CHMe_2$), 7.27–7.46 (m, 3, Ph), 7.47–7.66 (m, 2, Ph).

Ketone **6** was isolated in 69%, 48%, 66%, 71%, and 29% yields by methods B–F, respectively.

1,3-Diphenyl-2-propyn-1-one (7) was prepared by methods A and B. The crude product was chromatographed with 3:100 (v/v) ether/hexane to give 196 mg (94%) of **7** by both methods A and B as a light yellow liquid: bp 108 °C (0.1 mm) [lit.[31] bp 175 °C (7 mm)]; IR (CCl_4) 1635, 2190 cm^{-1}; NMR (CCl_4) δ 7.25–7.75 (m, 8, Ph), 8.05–8.26 (m, 2, Ph).

Low-temperature (−78 °C) crystallization of **7** from ether gave light yellow crystals, mp 47–47.5 °C (lit.[14] mp 49–50 °C).

1-(*p*-Nitrophenyl)-3-phenyl-2-propyn-1-one (8). Method A. The crude product was chromatographed with 1:1 (v/v) $CHCl_3$/hexane to give 143.4 mg (57%) of **8** as a brownish yellow solid: mp 160.2–160.7 °C (lit.[32] mp 159–160 °C); IR ($CHCl_3$) 1720, 2230 cm^{-1}; NMR ($CDCl_3$) δ 7.42–7.61 (m, 3, Ph), 7.65–7.78 (m, 2, Ph), 8.40 (s, 4, *p*-O_2NPh).

4-Phenyl-3-butyn-2-one (9). Method A. The crude product was chromatographed with 2:100 (v/v) ether/hexane to give 79 mg (55%) of **9** as a colorless liquid: bp 46 °C (0.11 mm) [lit.[31] bp 120–125 °C (14 mm)]; IR (CCl_4) 1670, 2090 cm^{-1}; NMR (CCl_4) δ 2.35 (s, 3, Me), 7.26–7.49 (m, 3, Ph), 7.50–7.70 (m, 2, Ph).

Ketone **9** was converted into its 2,4-dinitrophenylhydrazone, mp 185.6–187.3 °C (lit.[33] 186–186.5 °C).

6,6-Diethoxy-2-methyl-4-hexyn-3-one (10). Method A. The crude product was chromatographed with 5:100 (v/v) ether/hexane to give 139 mg (70%) of **10** as a colorless liquid: bp 51.5 °C (0.13 mm); IR (CCl_4) 1655, 2210 cm^{-1}; NMR (CCl_4) δ 1.20 (d, 6, J = 7.5 Hz, $CHMe_2$), 1.25 (t, 6, J = 7.5 Hz, OCH_2Me), 2.62 (septet, 1, J = 7.5 Hz, $CHMe_2$), 3.63 (complex m, 4, OCH_2Me), 5.29 (s, 1, $CH(OEt)_2$).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.54; H, 9.34.

5,5-Diethoxy-3-pentyn-2-one (11). Method A. The crude product was chromatographed with 4:100 (v/v) ether/hexane to give 52 mg (31%) of **11** as a colorless liquid: bp 34 °C (0.1 mm); IR (CCl_4) 1680, 2195 cm^{-1}; NMR (CCl_4) δ 1.23 (t, 6, J = 7.5 Hz, OCH_2Me), 2.33 (s, 3, COMe), 3.63 (complex m, 4, OCH_2Me), 5.28 (s, 1, $CH(OEt)_2$); mass spectrum, m/e (relative intensity) 170 (0.21), 169 (1.46), 155 (0.6), 141 (0.69), 127 (1.41), 126 (8.86), 125 (100), 113 (2.45), 110 (2.43), 103 (4.43), 99 (1.76), 98 (6.38), 97 (85.40), 75 (5.41), 71 (2.70), 55 (30.5), 54 (10.72), 47 (5.21), 46 (5.27), 45 (17.09), 43 (33.48), 31 (27.54), 29 (29.56).

We believe **11** is perfectly pure on the basis of thin-layer chromatography and NMR and mass spectrometry; however, it repeatedly gave elemental analyses that were high in carbon.

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4,4-Diethoxy-1-phenyl-2-butyn-1-one (12). Method A. The crude product was chromatographed with 5:100 (v/v) ether/hexane to give 158 mg (68%) of **12** as a light yellow liquid: bp 91 °C (0.07 mm); IR (CCl_4) 1640, 2210 cm^{-1}; NMR (CCl_4) δ 1.26 (t, 6, J = 7.5 Hz, OCH_2Me), 3.72 (complex m, 4, OCH_2Me), 5.34 (s, 1, $CH(OEt)_2$), 7.35–7.70 (m, 3, Ph), 8.06–8.24 (m, 2, Ph); mass spectrum, m/e (relative intensity) 232 (0.16), 231 (0.98), 203 (1.12), 188 (23.25), 187 (100), 160 (11.97), 159 (98.55), 157 (1.30), 155 (0.23), 131 (12.41), 129 (5.63), 127 (0.30), 105 (25.06), 103 (14.16), 89 (4.63), 81 (17.45), 77 (21.99), 59 (17.27), 53 (23.93), 51 (14.93), 45 (16.45).

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.41; H, 6.90. Found: C, 72.23; H, 7.22.

1-(Trimethylsilyl)-4-methyl-1-pentyn-3-one (13). Method A. The crude product was chromatographed with 1:100 (v/v) ether/hexane to give 120 mg (71%) of **13** as a colorless liquid: bp 23 °C (0.19 mm) [lit.[9] bp 78.2–81.80 °C (17 mm)]; IR and NMR spectra are identical with those previously reported.[9]

1-Phenyl-3-(trimethylsilyl)-2-propyn-1-one (14). Method A. The crude product was chromatographed with 2:100 (v/v) ether/hexane to give 128.9 mg (64%) of **14** as a pale yellow liquid: bp 64 °C (0.12 mm) [lit.[9] bp 98–99 °C (1 mm)]; IR and NMR spectra are identical with those previously reported.[9]

1-(*p*-Nitrophenyl)-3-(trimethylsilyl)-2-propyn-1-one (15). Method A. The crude product was chromatographed with 5:100 (v/v) ether/hexane to give 127 mg (51%) of **15** as a colorless solid: mp 132.2–132.7 °C (lit.[11b] mp 134–135 °C); IR ($CHCl_3$) 1667, 2128 cm^{-1}; NMR ($CDCl_3$) δ 0.36 (s, 9, $SiMe_3$), 8.32 (s, 4, p-O_2NPh).

5-[(*tert*-Butyldimethylsilyl)oxy]-3-pentyn-2-one (16). Method A. The crude product was chromatographed with 4:100 (v/v) ether/hexane to give 101 mg (48%) of **16** as a pale yellow liquid: bp 39 °C (0.08 mm); IR (CCl_4) 1683, 2192 cm^{-1}; NMR (CCl_4) δ 0.06 (s, 6, $SiMe_2$), 0.82 (s, 9, t-Bu), 2.19 (s, 3, COMe), 4.34 (s, 2, OCH_2); mass spectrum, m/e (relative intensity) 212 (0.29), 211 (0.49), 197 (1.69), 166 (0.41), 155 (39.23), 145 (7.66), 132 (2.79), 124 (38.24), 117 (8.67), 99 (2.58), 93 (3.84), 85 (2.34), 83 (11.83), 75 (100), 69 (1.72), 57 (6.27), 44 (29.31), 43 (21.72).

Anal. Calcd for $C_{11}H_{20}O_2Si$: C, 62.26; H, 9.43; Si, 13.21. Found: C, 61.96; H, 9.56; Si, 13.22.

6-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-4-hexyn-3-one (17). Method A. The crude product was chromatographed with 5:100 (v/v) ether/hexane to give 145 mg (60%) of **17** as a pale yellow liquid: bp 61 °C (0.15 mm); IR (CCl_4) 1670, 2195 cm^{-1}; NMR (CCl_4) δ 0.03 (s, 6, $SiMe_2$), 0.82 (s, 9, t-Bu), 1.08 (d, 6, J = 7.5 Hz, $CHMe_2$), 2.52 (septet, 1, J = 7.5 Hz, $CHMe_2$), 4.34 (s, 2, OCH_2); mass spectrum, m/e (relative intensity) 240 (0.01), 225 (0.34), 197 (0.93), 183 (9.73), 153 (5.68), 141 (5.15), 132 (0.22), 125 (2.60), 113 (5.85), 109 (12.79), 97 (1.93), 95 (1.09), 83 (10.42), 75 (100), 73 (23.17), 72 (1.96), 66 (3.14), 58 (24.75), 57 (5.54), 43 (89.55), 41 (13.48), 29 (7.71).

Anal. Calcd for $C_{13}H_{24}OSi$: C, 65.00; H, 10.00; Si, 11.67. Found: C, 64.71; H, 10.12; Si, 11.77.

4-[(*tert*-Butyldimethylsilyl)oxy]-1-phenyl-2-butyn-1-one (18). Method A. The crude product was chromatographed with 5:100 (v/v) ether/hexane to give 182 mg (66%) of **18** as a pale yellow liquid: bp 83.5 °C (0.08 mm); IR (CCl_4) 1661, 2225 cm^{-1}; NMR (CCl_4) δ 0.19 (s, 6, $SiMe_2$), 0.97 (s, 9, t-Bu), 4.64 (s, 2, OCH_2), 7.36–7.76 (m, 3, Ph), 8.06–8.26 (m, 2, Ph); mass spectrum, m/e (relative intensity) 274 (0.07), 231 (0.06), 217 (2.72), 187 (0.94), 169 (0.05), 153 (2.40), 145 (0.53), 132 (0.61), 131 (0.67), 105 (1.03), 93 (2.94), 75 (61.86), 58 (33.35), 43 (100).

Anal. Calcd for $C_{16}H_{22}O_2Si$: C, 70.07; H, 8.03; Si, 10.22. Found: C, 69.44; H, 8.11; Si, 10.47.

Methyl 5-Methyl-4-oxo-2-hexynoate (19). Method A. The crude product was chromatographed with 1:10 (v/v) ether/hexane to give 103 mg (67%) of **19** as a colorless liquid: bp 49.5 °C (0.68 mm); IR (CCl_4) 1675, 1705 cm^{-1}; NMR (CCl_4) δ 1.21 (d, 6, J = 7.5 Hz, $CHMe_2$), 2.67 (septet, 1, J = 7.5 Hz, $CHMe_2$), 3.83 (s, 3, CO_2Me); mass spectrum, m/e (relative intensity) 155 (0.77), 154 (0.78), 123 (28.78), 122 (36.01), 112 (56.60), 111 (31.30), 97 (21.14), 95 (23.89), 94 (29.28), 85 (16.01), 83 (6.56), 82 (34.24), 71 (25.40), 59 (19.80), 53 (33.84), 43 (100), 41 (57.58), 39 (36.41), 31 (76.85).

Anal. Calcd for $C_8H_{10}O_3$: C, 62.34; H, 6.49. Found: C, 61.96; H, 6.70.

Subjection of 9 to Reaction Conditions. (A) Treatment of **9** according to method A with the omission of the acyl chloride resulted in a 21% recovery of **9**.

(B) Treatment of **9** according to method A with the omission of both the acyl chloride and the stannane resulted in an 86% recovery of **9**.

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Registry No. 5a, 3757-88-8; **5b**, 81535-78-6; **5c**, 81353-38-0; **5d**, 81535-79-7; **5e**, 81535-80-0; **6**, 5923-10-4; **7**, 7338-94-5; **8**, 3672-66-0; **9**, 1817-57-8; **9** hydrazone, 1474-94-8; **10**, 81535-81-1; **11**, 55402-04-5; **12**, 53366-80-6; **13**, 53210-05-2; **14**, 13829-77-1; **15**, 17950-66-2; **16**, 81535-82-2; **17**, 81535-83-3; **18**, 81535-84-4; **19**, 81553-85-7; **20**, 10160-87-9; **21**, 76782-82-6; chlorotributylstannane, 1461-22-9; phenylacetylene, 536-74-3; methoxytributylstannane, 1067-52-3; (trimethylsilyl)acetylene, 1066-54-2; methyl propiolate, 922-67-8; p-nitrobenzoyl chloride, 122-04-3; acetyl chloride, 75-36-5; isobutyryl chloride, 79-30-1; benzoyl chloride, 98-88-4.

The Total Synthesis of Prostaglandins by the Tropolone Route

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A general synthesis from α-tropolone methyl ether of natural and modified prostaglandins is detailed. A key intermediate in the synthesis, 7-methoxybicyclo[3.2.0]hepta-3,6-dien-2-one, has been secured from α-tropolone methyl ether in improved yield and converted to an array of natural and modified prostaglandins through the use of a number of regio- and stereoselective reactions. In several instances, proof of structure and stereochemistry has been obtained through conversion of PGA_2 from the marine coral *Plexaura homomalla* to the synthetically derived products.

Introduction

The prostaglandins (PG), found naturally in mammals and some marine corals, exhibit a remarkably broad range of biological properties largely determined by the nature and stereochemistry of the functional groups located on the five-membered ring and on the two alkyl side chains.[2] In spite of the synthetic difficulties presented by these

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