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(10) It has been elegantly demonstrated by ^{18}O tracer studies that in the opening of a secondary–tertiary epoxide in the vitamin D series with acetic acid, acetate attack occurs at the tertiary center with retention of configuration at the secondary center, followed by transacetylation of the *tert*-acetyl group to the secondary alcohol: J. J. Partridge, S.-J. Shiuey, E. G. Baggiolini, B. Hennessy, and M. R. Uskokovic in "Proceedings of the Third Workshop on Vitamin D_3", W. deGruyter, Ed., New York, N.Y., 1977, p 47. Although firm evidence is lacking, it is probable that the facile acetyl migration of **11** to **13** is indicative of a cis relationship of the C-3 and C-4 oxygens.
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(12) Hydantoin configuration is easily established by NMR: $J_{H\text{-}5,6}$ (cis) = 4 Hz; $J_{H\text{-}5,6}$ (trans) = 11 Hz (see ref 11).
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Mercury in Organic Chemistry. 12.[1] Synthesis of β-Chloro-$\Delta^{\alpha,\beta}$-butenolides via Mercuration–Carbonylation of Propargylic Alcohols[2]

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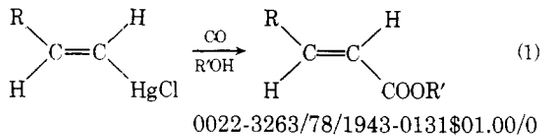
A number of propargylic alcohols react with mercuric chloride to give (*E*)-β-chloro-γ-hydroxyvinylmercuric chlorides. These can be readily carbonylated in a variety of solvents using stoichiometric amounts of palladium chloride and 1 atm of carbon monoxide to give essentially quantitative yields of the corresponding β-chloro-$\Delta^{\alpha,\beta}$-butenolides. Carbonylation can be effected using only catalytic amounts of palladium chloride if cupric chloride is used as a reoxidant and benzene as the solvent.

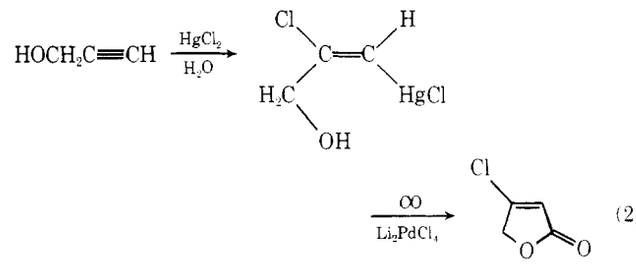
Unsaturated five-member ring lactones, butenolides, occur widely in nature[5] and possess an unusual range of biological activity.[6] They appear throughout the plant kingdom from the simple metabolites of lichens, mold, and fungi[7] to the more complex sesquiterpenes of the family Compositae[8] and steroidal glycosides of the families Ranunculaceae, Liliaceae, Scrophulariaceae, and Apocyanaceae.[9] More recently butenolides have been observed in such diverse animal species as sponges,[10-15] butterflies,[16] and insects.[17] In the latter species they appear to play a significant role as chemical defense weapons. Butenolides also hold promise as insecticides,[18] herbicides,[19] and seed and plant growth regulators.[20-22] Of considerable importance is their widespread allergenic,[23,24] antibacterial,[25,26] and antifungal[27-29] activity. Undoubtedly, vitamin C is the most physiologically important butenolide, but tremendous interest has also been generated by the cardiac glycosides which have the remarkable ability to reduce the frequency, but increase the amplitude of the heart beat.[9] Although in some cases carcinogenic,[30,31] an increasing number of butenolides exhibit cytotoxic and/or tumor inhibitory properties toward a variety of cancers.[32,33]

The unusual range of biological activity of butenolides has stimulated considerable research on the synthesis of these valuable compounds.[34] Of foremost interest are the $\Delta^{\alpha,\beta}$-butenolides. Recent work in our laboratory on the palladium promoted carbonylation of vinylmercurials (eq 1)[35] suggested



(1)

a novel new route to these butenolides. During that work we found that the β-chlorovinylmercurial[36] obtained by mercuric chloride addition to propargyl alcohol could be readily carbonylated to give β-chloro-$\Delta^{\alpha,\beta}$-butenolide [4-chloro-2(5*H*)-furanone] in 96% isolated yield (eq 2). The ease with which



(2)

both mercuration and carbonylation could be effected and the high yield of butenolide encouraged us to examine the full scope of both of these reactions. We wish now to report the complete experimental details of that investigation.

Results and Discussion

Mercuration of Propargylic Alcohols. The first step in our new approach to butenolides involves the mercuration of propargylic alcohols. Nesmeyanov and Kochetkov reported in 1949 that propargyl alcohol (55% yield), 2-methyl-3-butyn-2-ol (38%), 2-butyne-1,4-diol (87%), and 2,5-dimethyl-3-hexyne-2,5-diol (95%) readily react at room temperature with saturated aqueous solutions of sodium chloride

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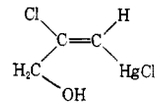
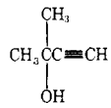
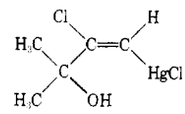
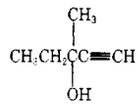
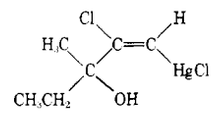
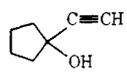
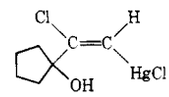
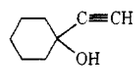
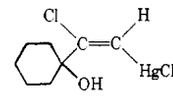
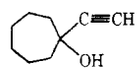
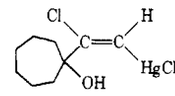
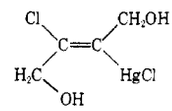
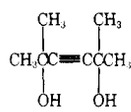
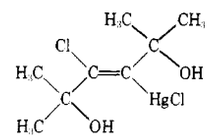
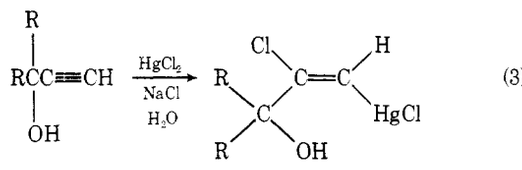
Table I. Mercuration of Propargylic Alcohols

Registry no.	Alcohol	Vinylmercurial	% isolated yield[a]	Mp, °C[a]
107-19-7	$HOCH_2C{\equiv}CH$		54 (55)	105 (105)
115-19-5			31 (38)	78 (70)
77-75-8			26	89-91
17356-19-3			37	104-105
78-27-3			31	137-138
2809-78-1			17	136-137
110-65-6	$HOCH_2C{\equiv}CCH_2OH$		45 (87)	120 (118)
142-30-3			85 (95)	93-220 (103)

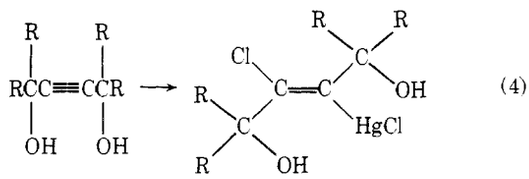
[a] Numbers in parentheses refer to ref 36.

and mercuric chloride to give the corresponding trans addition products in the yields indicated (eq 3, 4).[36] In repeating that



(3)

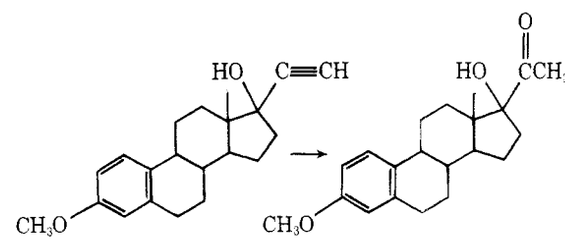
R = H, CH_3



(4)

R = H, CH_3

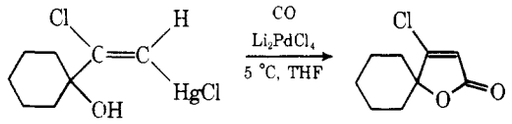
work we have generally gotten similar yields, except in the case of 2-butyne-1,4-diol, where we obtained a 45% yield. In the case of 2,5-dimethyl-3-hexyne-2,5-diol our product did not melt at 103 °C as indicated in the literature, but decomposed over a wide range (93–220 °C). Although the yields are not particularly good, the ease with which the compounds are prepared and isolated encouraged us to examine the mercuration of a whole range of propargylic alcohols. The results of that study are summarized in Table I. While we were able to obtain modest yields of vinylmercurials from several low molecular weight tertiary alcohols, increasing the molecular weight presented certain difficulties. The alcohols were no longer very soluble in the aqueous reaction mixture, and the addition of methanol as a cosolvent apparently not only increased the solubility of the propargylic alcohols, but the solubility of the vinylmercurials as well, and an insoluble white precipitate could no longer be obtained. Thus, the attempted mercuration of the tertiary alcohols 2-phenyl-3-butyn-2-ol, 3-methyl-1-heptyn-3-ol, 3-methyl-1-heptyn-6-en-3-ol, and 3-methyl-1-dodecyn-3-ol either gave no apparent reaction or the reaction mixtures turned dark. Similarly, many attempts to mercurate mestranol only gave starting material or the corresponding methyl ketone, although it appears that some of the desired vinylmercurial may have been formed (eq 5).



(5)

The attempted mercuration of several secondary alcohols (1-phenyl-2-propyn-1-ol, 3-butyn-2-ol, and 1-hexyn-3-ol) gave only dark reaction mixtures and no solid vinylmercurials. A closer look at these reactions by NMR (appearance of a vinyl proton in the correct region) suggested that some vinylmercurial was formed, but that for some reason it failed to precipitate. Thus, it appears that the desired trans addition products of mercuric chloride and propargylic alcohols are only formed and precipitate when relatively low molecular

Table II. Effect of Added Reagents



Reagent[a]	% yield[b]	Reagent[a]	% yield[b]
ZnF_2	47	Al_2O_3	79
	58	BaO	83
$MgSO_4$	61	Li_2CO_3	87
Na_2SO_4	66	K_2CO_3	94
$HC(OCH_3)_3$	68	CaO	95
HgO	76	MgO	95
NaOAc	76		

[a] 1 mmol of mercurial and 1 mmol of reagent. [b] All reactions were run until the maximum yield was obtained as determined by GLC analysis using an internal standard.

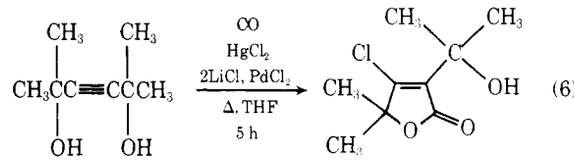
weight, symmetrically substituted propargylic alcohols are employed.

Several related reactions also failed. We were unable to obtain any vinylmercurial from propargyl alcohol when mercuric bromide and sodium bromide were employed, or when the corresponding iodides were used. Similarly the homopropargylic alcohol 3-butyn-1-ol also failed to give any β-chlorovinylmercurial under our usual reaction conditions.

Carbonylation of the β-Chloro-γ-hydroxyvinylmercurials. Although we were not able to prepare a large number of the desired vinylmercurials from mercuric chloride addition to propargylic alcohols, and the yields were often low, the mild reaction conditions and the facility with which this route leads to butenolides encouraged us to examine the carbonylation of these compounds as a simple route to butenolides. In our initial studies it became evident that these β-chloro-γ-hydroxyvinylmercurials are not as rapidly carbonylated as the simple vinylmercurials studied earlier,[35] and it therefore became unnecessary to start the reactions at −78 °C and to allow them to warm up slowly. Instead, we have found it convenient to run the reactions in a cold room at approximately 5 °C. We also observed, as indicated later, that the carbonylation reactions proceed well in most any solvent. We therefore switched from diethyl ether[35] to tetrahydrofuran (THF) for most reactions, because of the greater solubility of the mercurials in this solvent and the significantly increased rate of carbonylation.

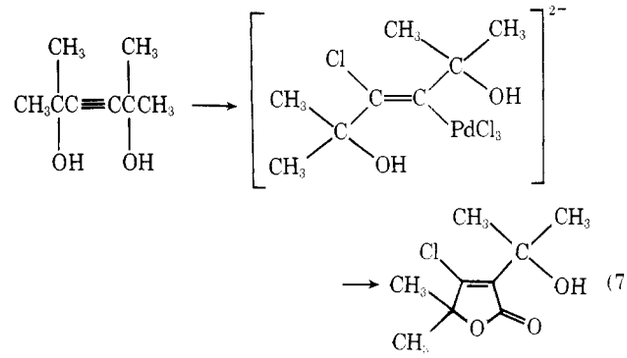
While the mercurials derived from propargyl alcohol (96% yield) and 2-methyl-3-butyn-2-ol (92%) were readily carbonylated using 1 equiv of palladium chloride, 2 equiv of anhydrous lithium chloride, 1 atm of carbon monoxide, THF as a solvent, a temperature of 5 °C, and a time of 24 h, the mercurial derived from 1-ethynylcyclohexanol gave only a 58% yield under these conditions. We reasoned that the lower yield might be due either to the 1 equiv of HCl generated during lactonization reacting with the tertiary allylic alcohol present in the starting mercurial or that the palladium chloride was so strongly coordinated to the alcohol group that it was no longer able to give rapid transmetalation with the mercurial moiety. This might in fact explain the slower rate of carbonylation of these alcohol-containing vinylmercurials. To examine these two possibilities we have run the carbonylation of the 1-ethynylcyclohexanol derived mercurial in the presence of a number of inorganic bases and drying agents, which might be expected either to react with HCl or more strongly to coordinate the hydroxy group, freeing the palladium for transmetalation (Table II). In line with this reasoning, all but one of the reagents used increased the yield, with the inorganic bases potassium carbonate, calcium oxide, and magnesium oxide providing the best results.

We have investigated the generality of this new carbonylation procedure using magnesium oxide by examining the carbonylation of the rest of the propargylic alcohol derived mercurials. In almost every case we have been able to obtain excellent yields of butenolides (Table III). However, the mercurial derived from 2,5-dimethyl-3-hexyne-2,5-diol gave none of the desired lactone under these conditions and only a 5% yield after 24 h at room temperature. On refluxing the reaction mixture, however, we were able to obtain a 94% yield of the desired butenolide. Since the starting mercurial in this case appears to decompose to mercuric chloride and the acetylene under these conditions, it appeared that we might be able to carbonylate the acetylenic diol directly by simply refluxing with all of the usual reagents. In fact, one can obtain a 92% yield in this fashion without isolating the intermediate mercurial (eq 6). Indeed, one can even omit mercuric chloride



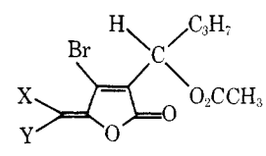
(6)

from the reaction and still obtain a 70% yield, although the reaction now requires approximately 20 h at reflux. No magnesium oxide is required in either of these reactions. Apparently dilithium tetrachloropalladate is itself able to add directly to the acetylene in a trans manner to give an intermediate vinylpalladium compound which is subsequently carbonylated and lactonized (eq 7). Previous workers have



(7)

studied the reaction of this same diol with aqueous solutions of the tetrachloropalladate dianion and reported a rather complex reaction product whose structure was assigned solely by infrared spectroscopy.[37] Later work also examined the analogous reaction of 2-methyl-3-butyn-2-ol.[38] Whatever intermediates are involved, this approach provides a very easy synthesis of the desired butenolide in one step from the commercially available diol. This particular butenolide is especially interesting due to its structural similarity to the acetoxyfimbrolides, a new class of halogenated lactones recently isolated from the red seaweed *Delisea fimbriata* and

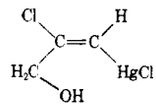
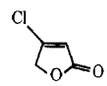
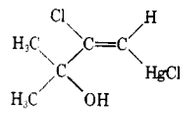
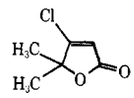
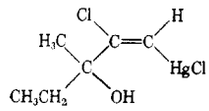
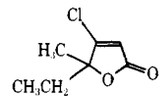
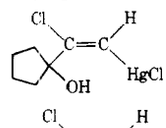
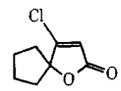
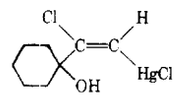
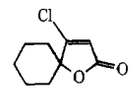
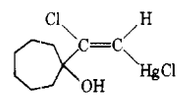
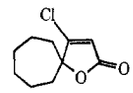
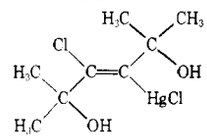
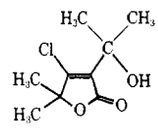


X, Y = H, Cl, Br, I

shown to have antimicrobial activity.[39,40] At present we are examining the scope of this new "direct" approach to butenolides.

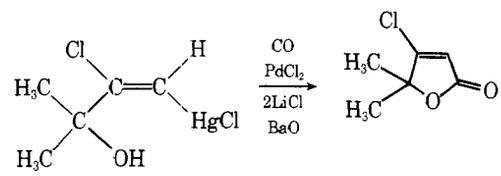
To date the only vinylmercurial which we have been unable to convert to the corresponding butenolide via carbonylation is the compound derived from 2-butyne-1,4-diol. Neither the

Table III. Synthesis of Butenolides via Carbonylation[a]

Registry no.	Mercurial	Butenolide	Registry no.	MgO[b]	% yield[c]	Mp, °C
56453-82-8			56453-85-1	—	(96)[d]	52-52.5[d]
63025-10-5			63025-15-0	—	92	66-66.5
				+	99 (88)	
63025-12-7			63025-16-1	+	98	64-64.5
63025-13-8			63025-17-2	+	99	36-36.5
63025-14-9			63025-18-3	—	58	55-55.5
				+	95 (92)	
63884-14-0			63884-15-1	+	81	~15-16
63025-11-6			63025-19-4	+	94[e]	102

[a] 1 mmol of $PdCl_2$, 2 mmol of LiCl, 10 mL of THF, 5 °C, 24 h. [b] 1 mmol or none. [c] Yields determined by GLC using an internal standard (isolated yields on a 5-mmol scale). [d] See ref 36. [e] Reaction run at reflux.

Table IV. Effect of Solvents on Carbonylation[a]



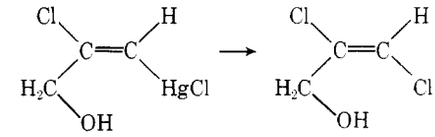
Solvent	% yield[b]	Reaction time, h[c]
Methanol	99	4
Acetone	95	<12
THF	99	24
Ether	99	36
Hexane	82	52[d]

[a] 1 mmol of mercurial, 1 mmol of $PdCl_2$, 2 mmol of LiCl, 1 mmol of BaO, 5 °C, 10 mL of solvent. [b] Yields determined by GLC using an internal standard. [c] Time required to reach maximum yield. [d] Reaction run at room temperature.

isolated mercurial nor our new direct approach gives the desired lactone. It certainly is not obvious to us at present why that should be so. The only product observed in these reactions is 4-chlorobutanol, a product of the direct reaction of THF and palladium chloride.

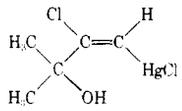
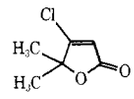
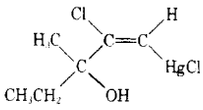
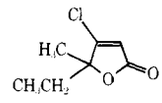
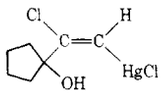
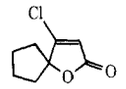
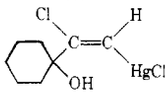
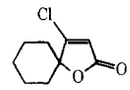
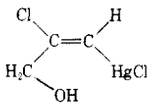
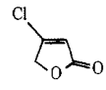
We have also examined the effect of several different solvents on the rates of lactone formation and the overall yield. As can be seen in Table IV, the polarity of the solvent makes little difference in the overall yield of the reaction, but dramatically affects the rate of butenolide formation. The more polar solvents give faster reactions, apparently due to increased solubility of the vinylmercurial and inorganic salts. These rates do not correlate well with the solubility of carbon monoxide in the indicated solvents, thus ruling out carbon monoxide as the rate-limiting reagent. It is indeed amazing that in hexane one can still obtain an 82% yield of butenolide even though none of the reagents are appreciably soluble in this solvent.

Palladium-Catalyzed Carbonylation. Although all of the above carbonylation reactions gave excellent yields using stoichiometric amounts of palladium chloride, it is obvious that the reaction would achieve even greater synthetic utility if a procedure could be developed requiring only catalytic amounts of palladium. In our early work with propargyl alcohol, we were able to obtain a 96% yield of β-chloro-$\Delta^{\alpha,\beta}$-butenolide using as little as 1% of either palladium chloride or 10% palladium on carbon, if we used anydrous cupric chloride as a reoxidant for palladium and diethyl ether as the solvent.[35] In scaling this reaction up from 10 to 50 mmol we found it necessary to carry out the reaction at 5 °C for several days (78% recrystallized yield). In THF, acetone, and methanol the major product was (*E*)-2,3-dichloro-2-propen-1-ol (eq 8). Even in ether the 2-methyl-3-butyn-2-ol derived

 (8)

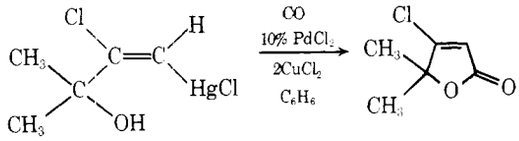
mercurial gave predominantly the *trans*-dichloro olefin. In fact, cupric chloride reacts readily with all of these vinylmercurials in polar solvents to give good yields of the corresponding dichloro olefins. Fortunately, we have been able to circumvent this undesirable side reaction by simply going to less polar solvents. Benzene proved ideal. Using 10% palladium chloride at room temperature in benzene without added

Table V. Palladium-Catalyzed Carbonylation[a]

Mercurial	% $PdCl_2$ catalyst	Reaction time, h	Butenolide	% yield[b]
	10	4		96[c]
	1	23		57[c]
	1	46		99
	10	24		100
	1	120		57
	10	19		93
	1	72		90
	10	19		(81)
	1	72		54
	1	432		77
	10	18		(78)[d]
	1	72		45[c]
	1	40		3

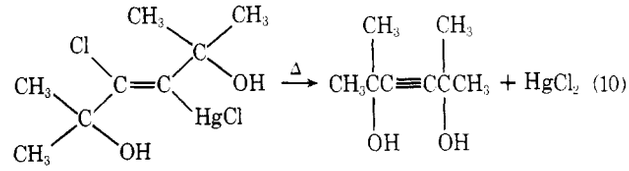
[a] 1 mmol of mercurial, 2 mmol of anhydrous $CuCl_2$, 1 mmol of MgO, 10 mL of benzene at room temperature. [b] GLC analysis using an internal standard (isolated, recrystallized yield). [c] No MgO present. [d] Isolated yield on a 50-mmol scale reaction using no MgO.

lithium chloride, we were able to obtain a 96% yield of the above butenolide in only 4 h (eq 9). While 1% palladium


(9)

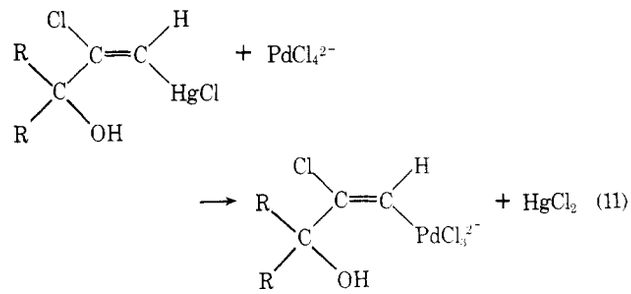
chloride catalyst gave only a 57% yield, the yield was increased to 99% by simply adding 1 equiv of magnesium oxide. Palladium on carbon proved less effective, giving only about 50% yields under similar conditions. Using this new catalytic procedure with either 1 or 10% palladium chloride and 1 equiv of magnesium oxide, in benzene, at room temperature, we have been able to obtain excellent yields of all of the previously prepared butenolides (Table V). In general 10% of the catalyst gives the best results. Surprisingly, this new catalytic procedure proved totally ineffective for the synthesis of β-chloro-$\Delta^{\alpha,\beta}$-butenolide. However, by omitting magnesium oxide we have been able to again achieve high yields of this particular butenolide. Obviously, there is a substantial difference in the effect of reaction conditions on the carbonylation of the tertiary alcohols vs. this primary alcohol.

Mechanism. The mechanism of the mercuric chloride addition to propargylic alcohols remains obscure. Since simple aliphatic terminal alkynes do not react with mercuric chloride under the reaction conditions employed in the mercuration of propargylic alcohols, it is obvious that the alcohol function plays an extremely important role in this reaction. Presumably the mercury salts are brought into the vicinity of the triple bond by coordination with the oxygen of the alcohol. It appears that the reaction is highly dependent on the steric environment of the alcohol and triple bond, and in a rather unusual way. The more sterically crowded tertiary alcohols react, while secondary alcohols give no precipitate at all. Since these reactions are most likely reversible, as indicated by the facile thermal decomposition of the mercurial derived from 2,5-dimethyl-3-hexyne-2,5-diol (eq 10), the insolubility of the

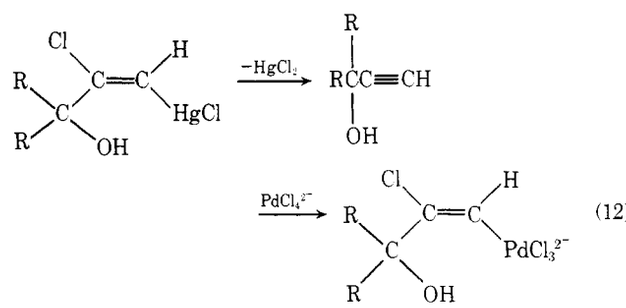

(10)

mercurial products may well determine the success or failure of the mercuration step. It is therefore not surprising that the more symmetrical propargylic alcohols give products, while the secondary alcohols possessing a chiral center fail to precipitate any mercurials at all.

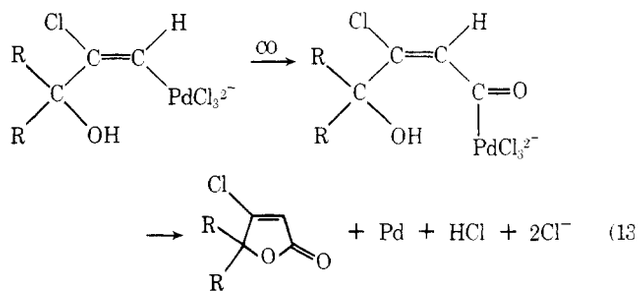
The carbonylation reaction presumably proceeds by an initial transmetalation reaction between the vinylmercurial and the palladium salt (eq 11), although it is possible that the


(11)

mercurial reversibly decomposes to the starting propargylic alcohol, which then adds the palladium salt in a trans manner (eq 12). Our results with the direct palladium chloride pro-


(12)

moted carbonylation of 2,5-dimethyl-3-hexyne-2,5-diol without mercuric chloride clearly indicate that the latter pathway is possible, but that it appears from our rate data to be a slower reaction and probably not a major pathway for generating the vinylpalladium intermediates. Once the vinylpalladium chloride or vinylpalladium trichloride dianion intermediates are formed, they probably immediately undergo carbon monoxide insertion and lactonization (eq 13). The


(13)

cupric chloride simply serves to reoxidize the palladium(0) back to palladium(II) chloride.

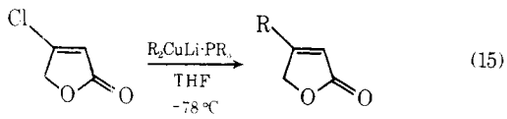
$$Pd + 2CuCl_2 \rightarrow PdCl_2 + Cu_2Cl_2 \quad (14)$$

The inorganic oxide or carbonate bases then entrap the HCl generated before it is able to destroy the tertiary allylic alcohol present in the vinylmercurial or -palladium intermediates.

Conclusion

Mercuric chloride readily adds to relatively low molecular weight propargylic alcohols containing either a primary or tertiary alcohol. Secondary alcohols do not precipitate vinylmercurial products. The resulting mercurials can be carbonylated in near quantitative yield by stirring with either an equivalent amount of palladium chloride and 2 equiv of lithium chloride under 1 atm of carbon monoxide at 5 °C in any of a variety of solvents, or better, with approximately 10% palladium chloride and 2 equiv of anhydrous cupric chloride in benzene at room temperature. The addition of magnesium oxide to these reactions generally substantially improves the yield of butenolide. In at least one case the carbonylation reaction can be carried out directly on the propargylic alcohol by simply refluxing all reagents together. We are presently examining the generality of this direct approach to the synthesis of β-chloro-$\Delta^{\alpha,\beta}$-butenolides.

The recent report of naturally occurring β-halo-$\Delta^{\alpha,\beta}$-butenolides possessing antimicrobial properties heightens interest in these compounds.[39,40] They also appear promising as intermediates for the synthesis of a wide varity of β-substituted butenolides, many of which might be expected to possess biological activity. For example, certain Gilman reagents appear to react instantaneously with the β-chloro-$\Delta^{\alpha,\beta}$-butenolides to give β-alkylbutenolides (eq 15). We are



(15)

presently studying a large number of these substitution reactions and hope to report on them before long.

Experimental Section

Reagents. All chemicals were used directly as obtained unless otherwise indicated. Propargyl alcohol, 1-ethynylcyclopentanol, and 3-methyl-1-pentyn-3-ol were purchased from Aldrich, and 2-methyl-3-butyn-2-ol, 2,5-dimethyl-3-hexyne-2,5-diol, and 1-ethynylcycloheptanol from Farchan. 1-Ethynylcyclohexanol was purchased from Matheson Coleman and Bell. Ether and THF were distilled from lithium aluminum hydride before use, while benzene was used directly as obtained from Fisher. The palladium chloride was generously supplied by Matthey Bishop, Inc., and Engelhard Industries. Mercuric chloride and anhydrous lithium chloride were purchased from Fisher and J. T. Baker, respectively. Cupric chloride (hydrated) was obtained from J. T. Baker and dried in a drying oven overnight at 130 °C before use.

The infrared and NMR spectra were recorded on a Beckman IR-4250 infrared spectrophotometer and Varian Associates A-60 NMR spectrometer, respectively. The mass spectra were obtained on an AEI MS-902 high-resolution mass spectrometer. Elemental analyses were performed by Galbraith Laboratories, Inc.

Mercuration of Propargylic Alcohols. All previously known propargylic alcohol derived mercurials were prepared according to the literature procedure.[36] All new mercurials were prepared as follows. A room-temperature saturated aqueous solution of mercuric chloride and sodium chloride (50 mL) (make certain the solution is saturated in both reagents) was placed in a water bath and 5 g of propargylic alcohol dissolved in 15 mL of methanol was added. After a few minutes of stirring, the solution became cloudy and a thick white precipitate formed. The mixture was stirred at room temperature for 1 h. The precipitate was collected by vacuum filtration and washed with a small amount of cold water. The solid was dried overnight at 0 °C in a vacuum desiccator, then ground up and dried one more day. The resulting powder was extracted with warm benzene and filtered by gravity. The filtrate was concentrated and then cooled to provide crystals.

The following β-chloro-γ-hydroxyvinylmercurials were prepared and characterized. (*E*)-2-Chloro-3-chloromercuri-2-propen-1-ol:[36] mp 105 °C (lit.[36] mp 105 °C); ^{1}H NMR (acetone-d_6) δ 3.2 (br s, 1, OH), 4.3 (d, 2, J = 1.8 Hz, CH_2), 6.27 (t, 1, J = 1.8 Hz, vinyl). (*E*)-3-Chloro-4-chloromercuri-2-methyl-3-buten-2-ol:[36] mp 78 °C (lit.[36] mp 70 °C); ^{1}H NMR (acetone-d_6) δ 1.5 (s, 6, CH_3), 5.05 (s, 1, OH), 6.01 (s, 1, vinyl). (*E*)-2-Chloro-1-chloromercuri-3-methyl-1-penten-3-ol: crude yield 36%, isolated yield 26%; mp 85–86 °C; ^{1}H NMR (acetone-d_6) δ 0.86 (t, 3, J = 7 Hz, $-CH_2CH_3$), 1.48 (s, 3, CH_3), 1.72 (q, 2, J = 7 Hz, CH_2), 4.84 (s, 1, OH), 6.06 (s, 1, vinyl). Anal. Calcd for $C_6H_{10}Cl_2HgO$: C, 19.57; H, 2.46. Found: C, 19.63; H, 2.62. (*E*)-1-(1-Chloro-2-chloromercuriethenyl)cyclopentanol: crude yield 81%, isolated yield 37%; mp 99–100 °C; ^{1}H NMR (acetone-d_6) δ 1.4–2.4 (m, 8, CH_2), 4.86 (s, 1, OH), 6.13 (s, 1, vinyl). Anal. Calcd for $C_7H_{10}Cl_2HgO$: C, 22.03; H, 2.64. Found: C, 21.86; H, 2.49. (*E*)-1-(1-Chloro-2-chloromercuriethenyl)cyclohexanol: crude yield 61%, isolated yield 31%; mp 137–138 °C; ^{1}H NMR (acetone-d_6) δ 1.3–2.0 (m, 10, CH_2), 4.5 (s, 1, OH), 6.03 (s, 1, vinyl). Anal. Calcd for $C_8H_{12}Cl_2HgO$: C, 24.28; H, 3.05. Found: C, 22.91; H, 2.82. (*E*)-1-(1-chloromercuriethenyl)cycloheptanol: crude yield 28%, isolated yield 17%; mp 136–137 °C; ^{1}H NMR (acetone-d_6) δ 1.4–2.4 (m, 12, CH_2), 5.07 (s, 1, OH), 6.10 (s, 1, vinyl). Anal. Calcd for $C_9H_{14}Cl_2HgO$: C, 26.38; H, 3.44. Found: C, 26.48; H, 3.49. (*E*)-2-Chloro-3-chloromercuri-2-butene-1,4-diol:[36] mp 120 °C (lit.[36] mp 118 °C); ^{1}H NMR (acetone-d_6) δ 3.18 (s, 1, OH), 4.3 (br s, 4, CH_2). (*E*)-3-Chloro-4-chloromercuri-2,5-dimethyl-3-hexene-2,5-diol:[36] mp 93–220°C (ethanol) (lit.[36] mp 103 °C); ^{1}H NMR (acetone-d_6) δ 1.41 (s, 12, CH_3), 3.55 (s, 1, OH).

Carbonylation of the β-Chloro-γ-hydroxyvinylmercurials. The butenolides were prepared according to the following representative procedure. Anhydrous lithium chloride (2 mmol, 0.085 g), 1 mmol of palladium chloride (0.178g), 1 mmol of magnesium oxide, and 10 mL of anhydrous THF were placed in a round-bottom flask with a septum inlet. While flushing with carbon monoxide at −78 °C, 1 mmol of the appropriate mercurial was added. A balloon filled with carbon monoxide was connected to the top of the flask, and the reaction mixture was allowed to warm up to ~5 °C and then stirred 24 h at that temperature. Saturated ammonium chloride solution (1 mL) and 10 mL of ether were added and stirring was continued for an additional hour at room temperature. The mixture was vacuum filtered, and the filtrate was washed with saturated potassium carbonate solution and dried over anhydrous sodium sulfate. After filtration and evaporation of the solvent, the crude product was recrystallized from pentane.

All yields determined by GLC analysis were run as above and an appropriate internal standard was added just prior to analysis. Internal standard correction factors were determined using authentic isolated butenolide samples. Isolated yields were obtained using both the above 1-mmol scale procedure and a 5-mmol scale procedure, in which case the yields were usually substantially higher.

The effect of various added reagents on the yield of butenolide obtained from carbonylation of (*E*)-1-(1-chloro-2-chloromercuriethenyl)cyclohexanol was studied by employing the 1-mmol procedure described above and substituting the appropriate reagents for magnesium oxide. The reactions were analyzed by GLC analysis using an internal standard and the results are summarized in Table II.

The effect of various solvents on the rate of formation and yield of butenolide in the carbonylation of (*E*)-3-chloro-4-chloromercuri-2-methyl-3-buten-2-ol was studied using a similar procedure, but employing 1 mmol of BaO as the added reagent and varying the solvent. The reactions were analyzed by GLC analysis using an internal standard and the results are summarized in Table IV.

The following new butenolides were prepared. 4-Chloro-5,5-dimethyl-2(5*H*)-furanone: isolated yield on a 1-mmol scale 59%, on a 5-mmol scale 88% (103% crude yield, mp 61–63 °C); mp 66–66.5 °C; ^{1}H NMR (CCl_4) δ 1.47 (s, 6, CH_3), 5.91 (s, 1, vinyl); IR (max) (KBr) 1776 (C=O), 1615 (C=C) cm^{-1}; *m/e* 146.0135 (calcd for $C_6H_7ClO_2$, 146.0138). 4-Chloro-5-ethyl-5-methyl-2(5*H*)-furanone: isolated yield on a 1-mmol scale 66%; mp 64–64.5 °C; ^{1}H NMR (CCl_4) δ 0.85 (t, 3, J = 7 Hz, $-CH_2CH_3$), 1.46 (s, 3, CH_3), 1.82 (q, 2, J = 7 Hz, CH_2), 5.9 (s, 1, vinyl); IR (max) (KBr) 1776 (C=O), 1615 (C=C) cm^{-1}; *m/e* 160.0288 (calcd for $C_7H_9ClO_2$, 160.0291). 4-Chloro-5,5-tetramethylene-2(5*H*)-furanone: isolated yield on a 1-mmol scale 63%; mp 36–36.5 °C; ^{1}H NMR (CCl_4) δ 1.6–2.0 (m, 8, CH_2), 5.9 (s, 1, vinyl); IR (max) (KBr) 1776 (C=O), 1617 (C=C) cm^{-1}; *m/e* (M − Cl, no parent observed) 137.0607 (calcd for $C_8H_9O_2$, 137.0603). 4-Chloro-5,5-pentamethylene-2(5*H*)-furanone: isolated yield on a 1-mmol scale 49%, on a 5-mmol scale 92% (105% crude yield, mp 52–56 °C); mp 55–55.5 °C; ^{1}H NMR (CCl_4) δ 1.4–2.0 (m, 10, CH_2), 5.91 (s, 1, vinyl); IR (max) (KBr) 1776 (C=O), 1615 (C=C) cm^{-1}; *m/e* 186.0453 (calcd for $C_9H_{11}ClO_2$, 186.0447). 4-Chloro-5,5-hexamethylene-2(5*H*)-furanone: isolated yield on a 1-mmol scale 45%; mp ~15–16 °C; ^{1}H NMR (CCl_4) δ 1.5–2.0 (m, 12, CH_2), 5.80 (s, 1, vinyl); IR (max) (KBr) 1776 (C=O), 1615 (C=C) cm^{-1}; *m/e* 200.0599 (calcd for $C_{10}H_{13}ClO_2$, 200.0604). 4-Chloro-5,5-dimethyl-3-(1-hydroxy-1-methylethyl)-2(5*H*)-furanone: prepared by refluxing the reaction mixture under carbon monoxide for 4 h; isolated yield on a 1-mmol scale 72%; mp 102 °C; ^{1}H NMR (CCl_4) δ 1.50 (s, 6, CH_3), 1.55 (s, 6, CH_3), 3.92 (s, 1, OH); IR

(max) (KBr) 1755 (C=O), 1645 (C=C) cm^{-1}; *m/e* (M − CH_3, no parent observed) 189.0298 (calcd for $C_8H_{10}ClO_3$, 189.0318). Anal. Calcd for $C_9H_{13}ClO_3$: C, 52.82; H, 6.40. Found: C, 53.02; H, 6.57.

In the direct carbonylation of 2,5-dimethyl-3-hexyne-2,5-diol, 1 mmol of acetylenic diol, 1 mmol of palladium chloride, 2 mmol of anhydrous lithium chloride, 1 mmol of mercuric chloride, and 10 mL of THF were mixed at room temperature and refluxed for 4 h under carbon monoxide. GLC analysis using an internal standard indicated a 92% yield of butenolide. Omission of mercuric chloride required that the reaction be refluxed for 20 h, but a 70% yield of butenolide could still be obtained under these conditions.

Palladium-Catalyzed Carbonylation. 4-Chloro-2(5*H*)-furanone (β-chloro-$\Delta^{\alpha,\beta}$-butenolide) was prepared on a 50-mmol scale using 10% palladium chloride as follows. To 5 mmol of palladium chloride (0.84 g), 100 mmol of lithium chloride (4.25 g), and 100 mmol of cupric chloride (13.45 g) in 250 mL of ether at −78 °C was added 50 mmol of (*E*)-2-chloro-3-chloromercuri-2-propen-1-ol (16.4 g). The flask was flushed with carbon monoxide and a large balloon filled with carbon monoxide was connected to the top of the flask. The cold bath was removed and the reaction mixture was stirred in a cold room (~5 °C) for 50 h. Saturated ammonium chloride solution (10 mL) was added and the mixture stirred an additional hour. The resulting suspension was vacuum filtered, washed with saturated ammonium chloride, and dried over anhydrous sodium sulfate. Evaporation of the ether afforded 6.18 g (105%) crude yield of product. Recrystallization from carbon tetrachloride provided a 78% isolated yield.

The 1-mmol scale catalytic carbonylation reactions summarized in Table V were carried out as follows. Anhydrous cupric chloride (2 mmol), the appropriate amounts of palladium chloride (0.01 or 0.10 mmol) and magnesium oxide (usually 1 mmol), and 5 mL of benzene were added to a round-bottom flask with septum inlet. After flushing with carbon monoxide and attaching a balloon full of carbon monoxide, an additional 5 mL of benzene containing 1 mmol of mercurial was added and the flask was stirred at room temperature for the appropriate length of time. An internal standard was then added and the reaction analyzed by GLC analysis. To determine the isolated yield of 4-chloro-5,5-pentamethylene-2(5*H*)-furanone on a 1-mmol scale, the catalytic carbonylation reaction was set up as described above and stirred for 19 h at room temperature. Then 1 mL of saturated ammonium chloride, 15 mL of ether, and charcoal were added. The mixture was stirred under carbon monoxide for 90 min longer, and the resulting suspension was filtered, washed with two 25-mL portions of saturated potassium carbonate, and dried over anhydrous sodium sulfate. Evaporation of the ether gave 0.3 g (112%) of crude product, which was then recrystallized from Skelly B in 81% isolated yield.

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Registry No.—Mercuric chloride, 7487-94-7; sodium chloride, 7647-14-5; (*E*)-2-chloro-3-chloromercuri-2-butene-1,4-diol, 63915-18-84.

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