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MERCURY IN ORGANIC CHEMISTRY. 35.[1] SYNTHESIS OF VINYLIC LACTONES FROM VINYLMERCURIALS AND ALKENOIC ACIDS VIA INTRAMOLECULAR π-ALLYLPALLADIUM DISPLACEMENT

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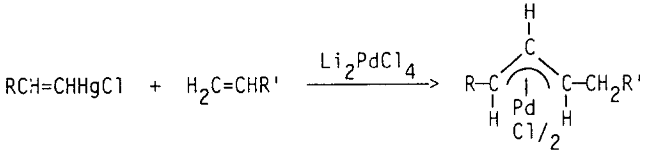
Summary: The reaction of vinylmercuric chlorides, Li_2PdCl_4 and 3-butenoic or 4-pentenoic acids, followed by refluxing with K_2CO_3, affords high yields of the corresponding γ-alkenyl-γ-butyro- or δ-alkenyl-δ-valerolactones by an intramolecular π-allylpalladium displacement process.

Five- and six-membered ring lactones substituted with a vinylic group in the five or six position respectively are common in nature and have proven useful as synthetic intermediates.[2-8] We recently reported a useful heteroannulation process[9] proceeding via intramolecular displacement of π-allylpalladium intermediates which suggested that such lactones might be prepared through analogous chemistry. We wish to report at this time the successful outcome of that investigation.

The reaction of vinylmercuric chlorides, Li_2PdCl_4 and acyclic alkenes affords π-allylpalladium compounds (eq. 1).[10] Intramolecular nucleophilic displacement on such compounds would be expected to afford cyclized products. Indeed, when an analogous reaction was effected using alkenoic acids, followed by refluxing with K_2CO_3, the anticipated five- and six-membered ring lactones were obtained in high yields (eq. 2). Some representative yields are reported in Table I.



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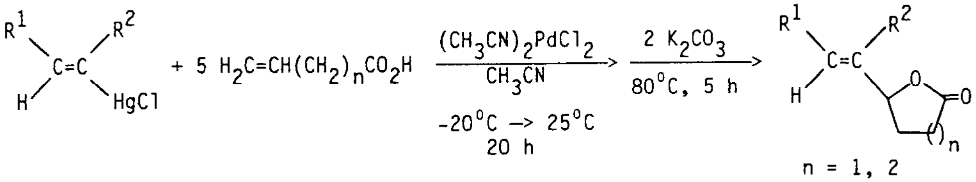
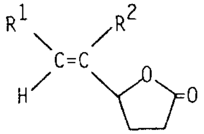
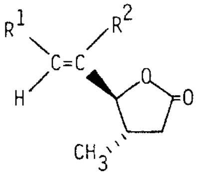
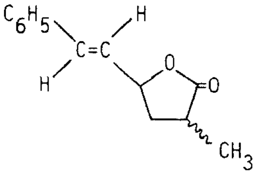


(2)

Table I. Synthesis of Vinylic Lactones[a]

Entry	Alkenoic Acid	Organomercurial		Lactone[b]
		R^1	R^2	(isolated yield, %)
				
1	H_2C=$CHCH_2CO_2H$	*n*-C_3H_7	H	51
2		*n*-C_8H_{17}	H	63
3		$(CH_3)_3C$	H	75
4		C_6H_5	H	67
5		$(CH_3)_3C$	CH_3	83
6		-$(CH_2)_4$-		85
				
7	H_2C=$C(CH_3)CH_2CO_2H$	C_6H_5	H	38
8		$(CH_3)_3C$	CH_3	42
				
9	H_2C=$CHCH(CH_3)CO_2H$	C_6H_5	H	72[c]

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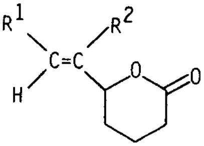
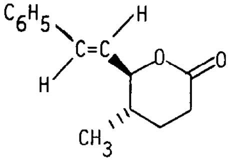
[a] All reactions were run by adding $(CH_3CN)_2PdCl_2$ (0.5 mmol), the vinylmercuric chloride (0.5 mmol), and the alkenoic acid (2.5 mmol) to 10 ml of CH_3CN at -20°C, and allowing the reaction to warm slowly to room temperature and to stir 20 h. Potassium carbonate (1 mmol) was then added and the reaction mixture was refluxed for 5 h before work-up.

[b] All new compounds gave correct ^{13}C and ^1H NMR, IR and exact mass or combustion analysis data.

[c] Cis/trans ratio = 55:45.

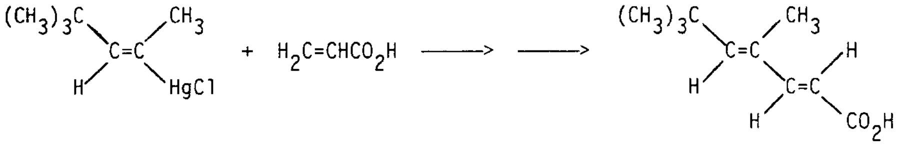
Table I. Continued

				
10	$H_2C{=}CH(CH_2)_2CO_2H$	$(CH_3)_3C$	H	68
11		$\underline{n}$-C_8H_{17}	H	59
12		C_6H_5	H	65
13		$(CH_3)_3C$	CH_3	70 (76[d])
				
14	$H_2C{=}C(CH_3)(CH_2)_2CO_2H$	C_6H_5	H	35

[d] Reaction run with $LiPdCl_3$.

The best yields of lactones were obtained using the more highly substituted vinylmercurials. In fact, vinylmercuric chloride itself failed to give any lactone product at all. This may result because the more sterically hindered vinylic palladium intermediates appear less prone to dimerize to 1,3-dienes.[11,12]

While 3-butenoic and 4-pentenoic acids gave excellent results, acrylic acid gave only the conjugated dienoic acid in about 50% yield (eq. 3). This may be due to the strain present in


(3)

the anticipated four-membered ring lactone, the inability of the carboxylate anion to reach either end of the intermediate π-allylpalladium species in order to undergo displacement, or particularly facile abstraction of the acidic hydrogen alpha to the carbonyl in this intermediate. We have also been unsuccessful in forming lactones from 5-hexenoic, 6-heptenoic and 10-undecenoic acids using the above procedure. In these cases, we have been able to isolate the expected π-allylpalladium products, but they do not cyclize under our usual reaction conditions or upon slow addition of 0.75 M solutions of these compounds to a solution of K_2CO_3 in refluxing acetonitrile.

The stereochemistry of this process is also noteworthy. While 3-methyl-3-butenoic acid (Table I, entries 7 and 8) and 4-methyl-4-pentenoic acid (entry 14) gave lower yields of the corresponding lactones, the product in each case consisted of a single stereoisomer, the trans product. This was established by close examination of the ^1H NMR coupling constants, nuclear Overhauser effects, and comparison with ^1H NMR data already in the literature. 2-Methyl-3-butenoic acid (entry 9), on the other hand, afforded a 55:45 mixture of cis and trans isomers respectively, as determined by comparison with ^1H and ^{13}C NMR data in the literature.

We are presently attempting to develop this overall process into one requiring only catalytic amounts of palladium and employing vinylic halides rather than vinylic mercurials. Preliminary experiments also suggest that we should be able to employ a variety of functionally substituted alkenes in this process and prepare cyclic ethers and carbocycles. We are presently pursuing these possibilities.

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References and Footnotes

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