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PALLADIUM COMPLEX-CATALYZED CARBONYLATION OF ORGANIC HALIDES IN THE PRESENCE OF CYCLIC ETHERS: HALOHYDRIN ESTER SYNTHESIS

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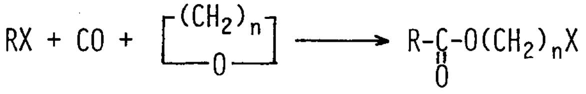
Summary: Cyclic ethers were cleaved by palladium complex-catalyzed carbonylation of organic halides to give halohydrin esters.

In a previous paper,[1] one of us reported acyl cyanides are efficiently synthesized via carbonylation of organic iodides in the presence of potassium cyanide (cyanocarbonylation). However, when this reaction was applied to benzyl chloride, the main product was not phenylacetyl cyanide, but 4-chlorobutyl phenylacetate, the 4-chlorobutyl group being derived from tetrahydrofuran used as the solvent. Other cyclic ethers with smaller rings were found to react more readily. We now wish to report the halohydrin ester synthesis via palladium complex-catalyzed carbonylation of organic halides in the presence of cyclic ethers.[2]

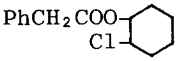
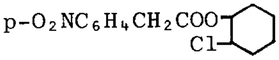


$$RX + CO + \left[(CH_2)_n \text{—} O \right] \longrightarrow R\text{-}\overset{O}{\overset{\|}{C}}\text{-}O(CH_2)_nX$$

The reaction of benzyl chloride with cyclohexene oxide is typical of the general procedure: Benzyl chloride (1 ml, 8.69 mmol), cyclohexene oxide (2 ml, used as the solvent), and iodophenylbis(triphenylphosphine)palladium (72.6 mg, 8.69×10^{-2} mmol) were placed in a 37 ml autoclave made of Hastelloy C, which was then charged with carbon monoxide (20 atm at room temperature). The mixture was stirred at 130°C until gas absorption ceased (ca. 16 h). The resulting mixture was distilled to give 1.24 g of 2-chlorocyclohexyl phenylacetate (57.4% isolated yield), bp 144-150°C/0.5 torr. Other examples are summarized in Table 1. Identity of product structures was established by NMR, IR, MS, analysis, and/or comparison (G.L.C.) with authentic samples prepared via different routes.

The table indicates that the present reaction can be successfully applied to aromatic, vinylic, benzylic halides, and the likes. The reaction could be effected under atmospheric pressure of carbon monoxide as well. Although the products of the reactions are also alkyl halides, their reactivity seems to be much less than that of those halides noted above. Therefore, halohydrin esters can be ob-

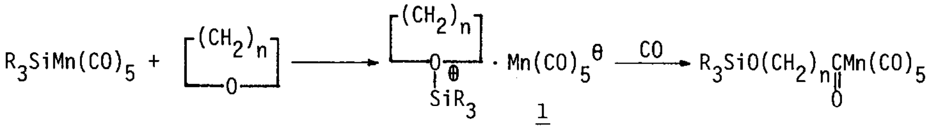
Table 1 Halohydrin Ester Synthesis via Carbonylation of Organic Halides in the Presence of Cyclic Ethers[a]

Halide	Ether[b]	Temp (C)	Time (h)	Product (Isomer ratio)[c]	Yield[d] (%)
$PhCH_2Cl$	PO	130	6	$PhCH_2COOCH(CH_3)CH_2Cl$ (70) $PhCH_2COOCH_2CH(CH_3)Cl$ (30)	49.5
$PhCH_2Cl$	CYO	130	16		71.9 (57.4)
$PhCH_2Cl$	TMO	130	11	$PhCH_2COO(CH_2)_3Cl$	43.6
$PhCH_2Cl$	THF	130	48	$PhCH_2COO(CH_2)_4Cl$	15.5
$PhCH_2Cl$[e,f]	THF	130	27	$PhCH_2COO(CH_2)_4Cl$	35.1
$PhCH_2Cl$	THP	130	49	$PhCH_2COO(CH_2)_5Cl$	3.5
$PhCH_2Cl$[e]	THP	130	22	$PhCH_2COO(CH_2)_5Cl$	8.1
$PhCH_2Cl$	$(n\text{-}C_4H_9)_2O$	130	20	$PhCH_2COOC_4H_9$	4.4
PhI	aq. PO	120	10	$PhCOOCH(CH_3)CH_2I$ (79) $PhCOOCH_2CH(CH_3)I$ (21)	69.3
PhBr	aq. PO	130	24	$PhCOOCH(CH_3)CH_2Br$ (67) $PhCOOCH_2CH(CH_3)Br$ (33)	13.5[g]
$p\text{-}CH_3COC_6H_4Br$	aq. PO	120	24	$p\text{-}CH_3COC_6H_4COOCH(CH_3)CH_2Br$ (68) $p\text{-}CH_3COC_6H_4COOCH_2CH(CH_3)Br$ (32)	(30.9)[h]
PhCH=CHBr	aq. PO	120	4	$PhCH{=}CHCOOCH(CH_3)CH_2Br$ (64) $PhCH{=}CHCOOCH_2CH(CH_3)Br$ (36)	69.9
$PhCH{=}CHCH_2Cl$[f]	EO	120	6	$PhCH{=}CHCH_2COO(CH_2)_2Cl$	74.6
$PhCOCH_2Cl$	aq. PO	120	2	$PhCOCH_2COOCH(CH_3)CH_2Cl$ (nd) $PhCOCH_2COOCH_2CH(CH_3)Cl$ (nd)	(67.3)
$p\text{-}O_2NC_6H_4CH_2Cl$[i]	CYO	120	24		(41.8)

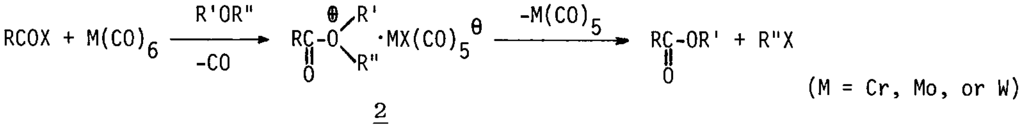
[a] Halide 4.35 mmol, ether 1 ml, $PhPdI(PPh_3)_2$ 4.35 × 10^{-2} mmol, p(CO) = 20 atm. [b] PO = propylene oxide, CYO = Cyclohexene oxide, TMO = trimethylene oxide, THF = tetrahydrofuran, THP = tetrahydropyran, EO = ethylene oxide; aq. PO is the one which was distilled under nitrogen without any drying agent. [c] Estimated by NMR. [d] The figures in parentheses are isolated yields. [e] The reaction was run in the presence of 10 μl of water. [f] $PdCl_2(PPh_3)_2$ was used as the catalyst in place of $PhPdI(PPh_3)_2$. [g] Conversion 14.3%. [h] Conversion 32.1%. [i] The reaction was effected under atmospheric pressure of carbon monoxide.

tained in fairly good yields. The reactivity of cyclic ethers decreased in the order, oxiran > oxetan > tetrahydrofuran > tetrahydropyran, as checked for benzyl chloride reactions. Dibutyl ether showed very low reactivity as compared with the cyclic ethers. This reactivity trend is parallel to that of ether cleavage of cyclic ethers by hydrogen halides.[3]

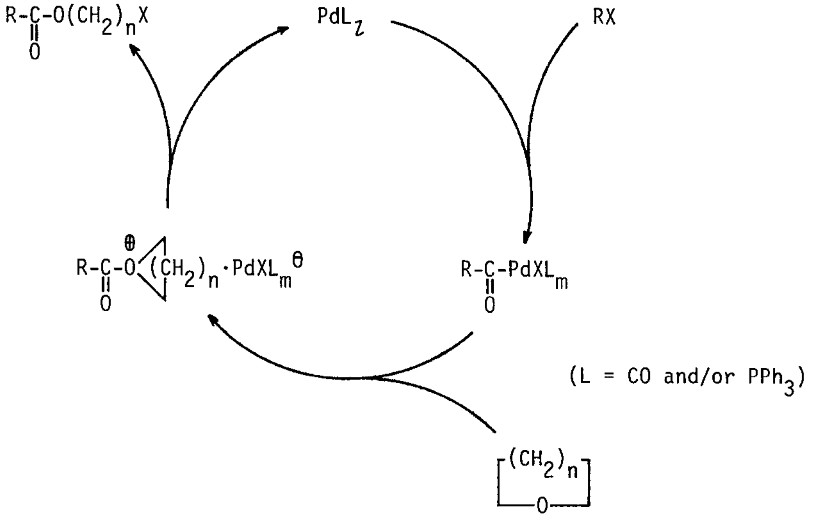
Very recently, Gladysz et al. reported that a trimethylsilylmanganese carbonyl complex reacts with cyclic ethers to give ω-trimethylsiloxyacylmanganese



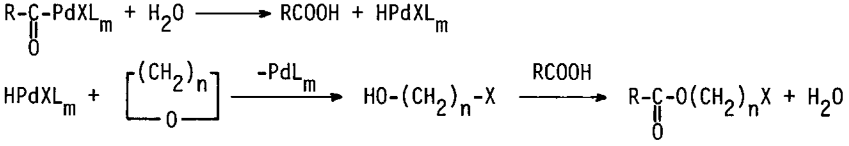
complexes.[4] In these reactions an ion pair 1 is postulated to be formed as an intermediate. A similar process is considered to work in polymerization of tetrahydrofuran by cobalt carbonyl-hydrosilane catalyst systems.[5] Group VI metal carbonyl-catalyzed acylative cleavage of ethers by acid chlorides is also considered to proceed through acyloxonium ion intermediate 2.[6] Acylpalladium species



seems to be electrophilic, as judged from their high reactivity towards nucleophiles such as alcohols, amines, organotin compounds, and potassium cyanide to give esters, amides, ketones, and acyl cyanides, respectively.[7] These precedents combined with the study by Heck et al.[8] may suggest the following tentative mechanism:



An alternative possibility that the moisture present in the system plays a role as a co-catalyst cannot be ruled out, for addition of a small amount of water to



$$R\text{-}\underset{\overset{\|}{O}}{C}\text{-}PdXL_m + H_2O \longrightarrow RCOOH + HPdXL_m$$

$$HPdXL_m + \left[\begin{smallmatrix}(CH_2)_n\\ O\end{smallmatrix}\right] \xrightarrow{-PdL_m} HO\text{-}(CH_2)_n\text{-}X \xrightarrow{RCOOH} R\text{-}\underset{\overset{\|}{O}}{C}\text{-}O(CH_2)_nX + H_2O$$

the system facilitated benzyl chloride reactions.

Oxirans are reported to react with acylnickel species generated by the reaction of organic halides with nickel carbonyl used as a reagent.[9] The present method constitutes a catalytic version of the same transformation and covers wider range of cyclic ethers.

In relation to this halohydrin ester synthesis, we recently found that even tertiary amines are susceptible to electrophilic attack by acylpalladium species to give tertiary amides. This amide formation and the full detail of halohydrin ester synthesis will be the subjects of coming papers.

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