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SYNTHESIS OF UNSATURATED HYDROXY ACIDS BY THE COBALT CARBONYL AND PHASE TRANSFER CATALYZED CARBONYLATION OF VINYL EPOXIDES

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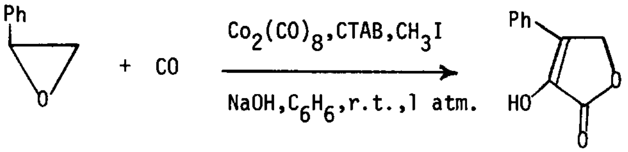
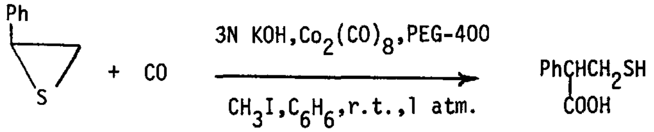
Summary: Phase transfer catalyzed reaction of vinyl epoxides with carbon monoxide, methyl iodide, catalytic amounts of cobalt carbonyl and TDA-1, affords β-hydroxy acids. High regioselectivity was observed in some cases.

Phase transfer catalysis is a valuable method for effecting metal catalyzed processes under remarkably mild conditions.[2] One of the most intensively investigated class of reactions are carbonylation reactions. It is known that methyl iodide can react with cobalt carbonyl or the cobalt tetracarbonyl anion and carbon monoxide, under phase transfer conditions, to generate acylcobalt tetracarbonyl.[3] The latter species is reactive towards a range of unsaturated and strained ring substrates.[4]

In 1985 one of us described the fascinating cobalt carbonyl and phase transfer catalyzed double carbonylation of styrene oxides. For instance, styrene oxide reacts with carbon monoxide, methyl iodide, aqueous sodium hydroxide, benzene as the organic phase, and cetyltrimethylammonium bromide (CTAB) as the phase transfer agent to give the enol tautomer of 4,5-dihydro-4-phenylfuran-2,3-dione (eq. 1).[5] Use of the sulfur analog as the reactant, i.e. 2-phenylthiirane, resulted in regiospecific monocarbonylation to the β-mercapto acid, the best yields being realized using potassium hydroxide as the base, and polyethylene glycol (PEG-400) as the phase transfer agent (eq. 2).[6]



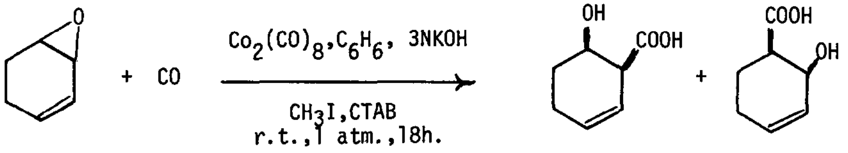
(eq. 1)



(eq. 2)

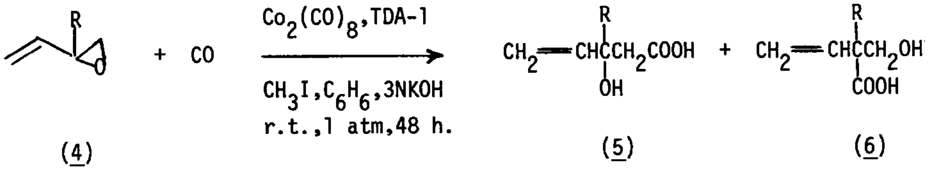
It was of interest to examine the use of vinylic epoxides, which are either commercially available or readily prepared, as substrates for the phase transfer carbonylation reaction catalyzed by cobalt carbonyl. Double carbonylation or ring cleavage and monocarbonylation to the hydroxy acid are the most probable reaction courses for such reactants. We now communicate the interesting results of this study.

When 1,2-epoxy-1,3-cyclohexadiene [1-also named as 7-oxabicyclo[4.1.0]hept-2-ene][7] was reacted with carbon monoxide, methyl iodide, potassium hydroxide (3N), benzene and catalytic amounts of CTAB and cobalt carbonyl for 18 hours at room temperature and one atmosphere, 6-hydroxy-2-cyclohexenecarboxylic acid (2) and 2-hydroxy-3-cyclohexenecarboxylic acid (3) were formed in a combined yield of only 18%, the ratio of 2/3 being 95/5. Modest improvement in yields were attained using Aliquat 336 (24%) or PEG-400 (23%) as the phase transfer agent, but tris dioxa-3,6-heptylamine (known as TDA-1)[8] was superior affording 2 and 3 in 35% yield. The yield of products increased to 48% by extending the reaction time to 60 hours, with high regioselectivity for the β,γ-unsaturated acid 2 [97/3 ratio of 2/3]. Methyl iodide and cobalt carbonyl are essential for this reaction, as the vinylic epoxide was recovered unchanged in tha absence of either component. Benzyl bromide could be used in place of methyl iodide but the yield of hydroxy acids was just 11%. The use of a lower base concentration [e.g. 1NKOH-10% yield] or a polar organic phase [e.g. 4-methyl-2-pentanone] is detrimental to the reaction. Stoichiometric quantities of cobalt carbonyl do not improve product yields.



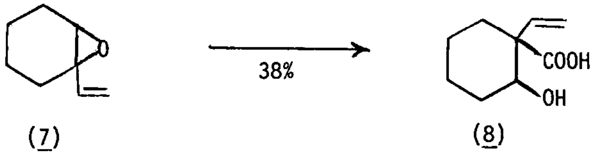
(1) (2) (3)

Several other vinyl epoxides were also subjected to carbonylation using cobalt carbonyl and TDA-1. Reasonable yields of unsaturated β-hydroxy acids resulted using the monoepoxide of butadiene (4, R=H) and isoprene (4, R=CH$_3$),[9] the reaction being regiospecific for 4, R=H



R = H(49%) 100 0
R = CH_3(53%) 85 15

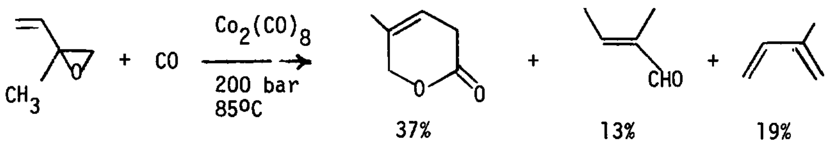
and regioselective for 4, R=CH_3. No selectivity was found when epoxyethyl 1-~~cycloh~~exene[10,11] was employed as the substrate (i.e. a 1:1 mixture of isomeric hydroxy acids) while 1-vinyl-7-oxabicyclo[4.1.0]heptane (7)[7] afforded only 2-hydroxy-1-vinylcyclohexanecarboxylic acid (8),



in which the double bond is attached to the carbon atom bearing the carboxylic group.

Let us compare the present phase transfer catalyzed carbonylation reaction with other vinyl epoxide-metal carbonyl processes. Irradiation of vinyl epoxides with iron pentacarbonyl affords lactone-iron tricarbonyl complexes which can be carbonylated to mixtures of unsaturated δ-lactones. Unfortunately, excess iron carbonyl is required to prepare the complex and drastic conditions [200 bar, 75°C] are necessary for the carbonylation step.[12] Both β- and δ-lactones can result on reaction of the ferralactone complexes with ceric ion in alcohol or acetonitrile.[7] β-Hydroxy acids can, or course, be formed from base promoted ring opening of β-but not δ-lactones.

There is one report of the carbonylation of a vinyl epoxide catalyzed by cobalt carbonyl (no CH_3I or base) but stringent conditions are necessary and a mixture of δ-lactone and ring-opened products are formed (eq. 3).[12] One or more of these products were obtained by the use



(eq. 3)

of palladium, platinum, or rhodium complexes as catalysts, at a pressure of 200-300 bars and at 75-90°C. δ-Lactones, or the hydroxy acids derived therefrom, were not detected in any reactions examined in the present study. Furthermore, the cobalt carbonyl phase transfer catalyzed process occurs under exceptionally mild conditions [room temperature, 1 atmosphere] and gives unsaturated β-hydroxy acids, usually with high regioselectivity.

The following procedure is representative: carbon monoxide was bubbled through a stirred solution of 3NKOH [15 ml.] containing 0.194 g. [0.60 mmol] of TDA-1. After 15 minutes, a degassed solution of cobalt carbonyl [0.171g., 0.50 mmol] was added, followed one hour later by methyl iodide [2.0 ml.] and thirty minutes later by a benzene (5 ml) solution of 0.140 g. [2.0 mmol] of **4**, R=H. The reaction mixture was stirred for 48 hours at room temperature and 1 atmosphere. The phases were separated and the aqueous phase was acidified (1N HCl) and extracted with ether (4x25 ml.). The dried ($MgSO_4$) ether extracted was rotary evaporated, and the resulting oil was purified by preparative thin-layer chromatography (silica gel), with methanol, affording 0.115 g (49%) of pure 3-hydroxy-4-pentenoic acid (**5**, R=H)[13]: ir($CHCl_3$) 3520-2500(COOH, OH), 1720(CO) cm^{-1}; nmr($CDCl_3$) δ 2.59(2H, CH_2), 4.32(1H, CHOH), 4.85-5.80 (4H, $CH=CH_2$ and OH), 11.00(1H, COOH); ms(m/e): 260$[M]^+$ of bistrimethylsilyl derivative. The methyl analog **5**, R=CH_3, had the following spectral properties: ir($CHCl_3$) 3500-2500(OH, COOH), 1720(CO) cm^{-1}; nmr ($CDCl_3$) δ 1.47(3H, CH_3), 2.74(2H, CH_2), 3.68(1H, OH), 5.04-5.80(3H, $CH=CH_2$), 12.00(1H, COOH); ms(m/e) 274$[M]^+$ of bistrimethylsilyl derivative.

Acknowledgments

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