Homogeneous Metal-Catalyzed Sequential Rosenmund–Tishchenko Reactions

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Esters can be isolated in good yields by the reaction of acid chlorides with hydrogen in the presence of 2,4,6-collidine and catalytic quantities of either $(Ph_3P)_3Ru(H)Cl$ or $(Ph_3P)_3RuCl_2$ in toluene. Acylruthenium hydrides are possible reaction intermediates.

The Rosenmund reduction[1,2] (heterogeneous Pd-catalyzed hydrogenolysis of acid chlorides to aldehydes) and the Tishchenko reaction[3,4] (aldehyde dimerization to esters) are of significant importance in synthetic organic chemistry.

Rosenmund reaction

$$RCOCl + H_2 \xrightarrow{Pd/BaSO_4} RCHO + HCl$$

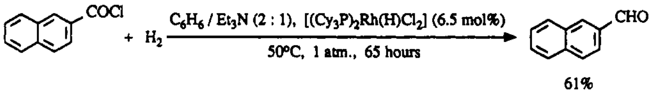
Tishchenko reaction

$$2RCHO \xrightarrow{Al(OEt)_3} RCOOCH_2R$$

Barium sulfate or charcoal-supported palladium is the usual catalyst for the Rosenmund reduction.[2] The homogeneous palladium-catalyzed hydrogenolysis of *m*-(trifluoromethyl)benzoyl fluoride (Et_3N; $P(H_2)$ = 55–100 bar; P(CO) = 1–90 bar; 175 °C; 6 h) was recently described, affording the corresponding aldehyde in 0.5–25% yield.[5] To our knowledge, no reports have appeared on the homogeneously catalyzed Rosenmund reaction between acid chlorides and H_2. The Tishchenko dimerization is usually catalyzed by aluminum alkoxides;[4] however, boric acid,[6] $LiWO_2$,[7] $Na_2Fe(CO)_4$,[8] and some hydridoruthenium complexes[9] have also been shown to induce this process. The main goal of the present work was to develop a selective method for the homogeneous transition-metal-catalyzed Rosenmund-type hydrogenolysis and a one-pot synthesis of esters from acid chlorides and H_2 based on sequential Rosenmund and Tishchenko reactions.

Results and Discussion

Recently it was shown that highly reactive coordinatively unsaturated rhodium species generated by reductive elimination of HCl from chloro hydrido complexes $[L_2Rh(H)Cl_2]$(L = *i*-Pr_3P, Cy_3P) under phase-transfer catalysis (PTC)[10] and biphasic[11] conditions efficiently catalyze hydrogenolysis of the C–Cl bond in chloroarenes.[12] It seemed reasonable to apply this system to the hydrogenolysis of a carbon–chlorine bond in acid chlorides. Obviously, the reaction conditions must have been significantly modified, due to high reactivity of acid chlorides toward many bases, including alkali and water. In other words, it was necessary to select a strong base possessing low nucleophilicity, which strongly binds HCl, but does not react with acid chlorides. The following bases have been tested: triethylamine, 1,8-bis(dimethylamino)-naphthalene (Proton Sponge), diisopropylethylamine, 2,4,6-collidine, activated molecular sieves, potassium carbonate, sodium bicarbonate, and calcium hydroxide. 2-Naphthaldehyde was obtained in 61% isolated yield starting from 2-naphthoyl chloride, H_2, and triethylamine. Naphthalene (3.5% yield) was a byproduct of this transformation.



The reaction of benzoyl chloride under the same conditions resulted in the formation of benzaldehyde in 30% yield (GLC). Unfortunately, even lower yields (0–15%) of aldehydes were obtained in the case of other aromatic acid chlorides. The process is sensitive to the nature of the base, with no reaction of benzoyl chloride observed by the use of Proton Sponge, K_2CO_3, or molecular sieves. Sodium bicarbonate and calcium hydroxide caused the hydrolysis of acid chlorides. Collidine and diisopropylamine gave lower yields of the desired products than triethylamine. The temperature of the reaction should not be higher than 50–60 °C, otherwise extensive decarbonylation[13] and catalyst poisoning occurs.

In the search for a more efficient catalyst for the homogeneous Rosenmund-type reduction, we found that the well-known chlorohydridoruthenium complex $[(Ph_3P)_3Ru(H)Cl]$ is able to catalyze both the Rosenmund reduction and the Tishchenko dimerization.

Since the reaction conditions (H_2, base) are suitable for the conversion of tris(triphenylphosphine)ruthenium dichloride to the tris(triphenylphosphine)ruthenium chlorohydride,[14] both complexes were tried as the catalysts. As

$$2ArCOCl + 2H_2 \xrightarrow[\text{toluene, 1 atm, 55 °C, 15–24 h, }-2HCl]{[(Ph_3P)_3Ru(H)Cl]\text{, 2,4,6-collidine}} \begin{matrix} ArCH_2COOAr \\ 52\text{–}85\% \end{matrix}$$

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Table I. Ruthenium-Catalyzed Synthesis of Esters from Acid Chlorides[a]

$$2RCOCl + 2H_2 \xrightarrow[-2HCl]{[Ru]} RCOOCH_2R$$

R	[Ru]	time, h	isolated yield, %	IR:[b] ν_{CO}, cm^{-1}	^1H NMR: δ ($CDCl_3$)
C_6H_5	$(Ph_3P)_3RuCl_2$	19	75	1719	5.35 (s, 2 H, CH_2); 7.2–8.1 (m, 10H)
	$(Ph_3P)_3Ru(H)Cl$	20	85		
p-$CH_3C_6H_4$	$(Ph_3P)_3RuCl_2$	20	85	1717	2.33 (s, 3 H, CH_3); 2.38 (s, 3 H, CH_3); 5.28 (s, 2 H, CH_2); 7.1–8.0 (m, 8 H)
m-$CH_3C_6H_4$	$(Ph_3P)_3RuCl_2$	21	77	1719	2.35 (s, 3 H, CH_3); 2.38 (s, 3 H, CH_3); 5.30 (s, 2 H, CH_2); 7.1–8.0 (m, 8 H)
o-$CH_3C_6H_4$	$(Ph_3P)_3RuCl_2$	20	52	1716	2.40 (s, 3 H, CH_3); 2.60 (s, 3 H, CH_3); 5.35 (s, 2 H, CH_2); 7.1–8.0 (m, 8 H)
2-naphthyl[c]	$(Ph_3P)_3RuCl_2$	24	61	1710	5.60 (s, 2 H, CH_2); 7.4–8.7 (m, 14 H)
1-naphthyl[d]	$(Ph_3P)_3RuCl_2$	24	55	1701	5.90 (s, 2 H, CH_2); 7.4–9.0 (m, 14 H)
	$(Ph_3P)_3Ru(H)Cl$	15	55		
p-ClC_6H_4[e]	$(Ph_3P)_3RuCl_2$	20	52	1712	5.30 (s, 2 H, CH_2); 7.3–8.1 (m, 4 H)
	$(Ph_3P)_3Ru(H)Cl$	15	53		
p-$CH_3OC_6H_4$	$(Ph_3P)_3RuCl_2$	22	ca. 25[f]	1710	3.79 (s, 3 H, CH_3); 3.82 (s, 3 H, CH_3)
	$(Ph_3P)_3Ru(H)Cl$	19	57		5.25 (s, 2 H, CH_2); 6.8–8.1 (m, 4 H)
p-$O_2NC_6H_4$[g]	$(Ph_3P)_3Ru(H)Cl$	24	67	1720	5.50 (s, 2 H, CH_2); 7.5–8.4 (m, 8 H)
2-furyl	$(Ph_3P)_3Ru(H)Cl$	21	ca. 10[f]	1725	5.25 (s, 2 H, CH_2); 7.1–7.8 (m, 6 H)

[a] Reaction conditions: 1 mmol of acid chloride, 2 mmol of collidine, 0.05 mmol of [Ru], 2 mL of toluene, H_2 (1 atm), 55 °C (oil bath). [b] Nujol mull for solids, neat compound for liquids. [c] mp 95 °C (from hexane). Anal. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16. Found: C, 84.84; H, 5.38. [d] mp 76–77 °C (from hexane). [e] mp 70–72 °C (see ref 15). [f] ^1H NMR yield.

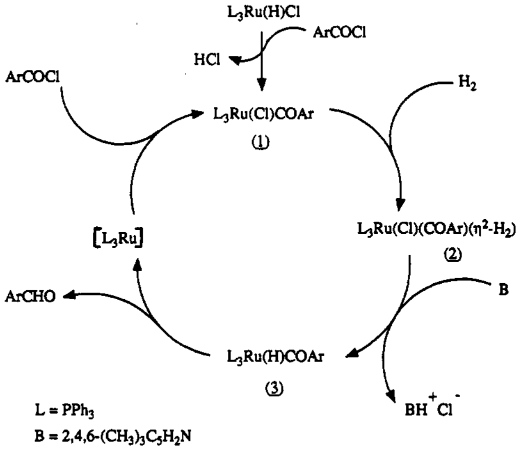
shown in Table I, in some cases the chlorohydridoruthenium complex indeed can be quite successfully replaced by its precursor, [$(Ph_3P)_3RuCl_2$]. These transformations represent the first example of a one-pot consecutive Rosenmund and Tishchenko reaction. Almost no difference in ester yields was found when the ruthenium dichloride was used instead of the ruthenium chlorohydride as the catalyst for the reactions of 4-chlorobenzoyl and 1-naphthoyl chlorides. However, the replacement of [$(Ph_3P)_3Ru(H)Cl$] for [$(Ph_3P)_3RuCl_2$] led to slight or even dramatic changes in yields of benzyl benzoate and 4,4′-dimethoxybenzyl benzoate, respectively.

A number of aroyl chlorides containing electron-withdrawing and electron-donating substituents have been successfully converted into the corresponding esters, which were characterized by ^1H NMR and IR spectral data (see Table I). However, aliphatic carboxylic acid chlorides (e.g., CH_3COCl and c-$C_6H_{11}COCl$) did not produce any ester under the same conditions. Neither reduction of the nitro group nor hydrogenolysis of the aromatic carbon–chlorine bond occurred when 4-nitrobenzoyl chloride and 4-chlorobenzoyl chloride, respectively, were subjected to the reaction. Earlier it was shown that the complex [$(Ph_3P)_3RuCl_2$] in the presence of aqueous alkali does not catalyze any reaction between nitroarenes and hydrogen,[17] unless quite drastic conditions are used (80–90 atm, 120–125 °C).[18]

Arenes (5–10% yield), arising from reductive decarbonylation of the starting acid chlorides, are byproducts of the reaction. Sometimes carboxylic acid anhydrides are also formed, when the conversion of the starting acid chloride is far from quantitative (the reaction is difficult to follow). In the presence of 2,4,6-collidine the remaining acid chloride produces the corresponding anhydride upon hydrolysis during workup.

Several mechanisms can be considered for the ruthenium-catalyzed reductive dimerization of acid chlorides leading to esters. Scheme I describes a possible mechanism for the catalytic hydrogenolysis of the carbon–chlorine bond in acid chlorides. The reductive elimination of HCl from the starting hydridoruthenium chloride, followed by oxidative addition of an aroyl chloride, may afford **1**. A similar transformation, with H_2 playing the role of the acid chloride, has already been published.[10] Addition of dihydrogen to the pentacoordinated compound **1** would give η^2-H_2 octahedral ruthenium(II) complex **2**. Transition-metal dihydrogen complexes (including many "nonclassical" ruthenium hydrides) have become quite common in organometallic and coordination chemistry over the last seven years.[19] Both cationic[20] and neutral[21] ruthenium η^2-H_2 complexes are readily deprotonated, and deprotonation of **2** with 2,4,6-collidine followed by elimination of Cl^- leads to the acylruthenium hydride **3**, which then eliminates the aldehyde.

Scheme I



The catalytic dimerization of the formed aldehyde can proceed via two pathways similar to those proposed in ref 9. Indeed, when benzaldehyde was allowed to react under the same conditions, benzyl benzoate (40% yield) was isolated from the reaction mixture after 4 h (the conversion

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of benzaldehyde was 100%; no reaction occurred in the absence of the ruthenium catalyst). Therefore, the rate of aldehyde dimerization is significantly higher than the rate of acid chloride hydrogenolysis (see Table I for reaction times). The absence of aldehydes among the reaction products, even when the conversion of starting acid chloride was far from completion, confirms this conclusion. Another mechanism *not* involving the generation of free aldehyde should also be considered. Complex **3** (Scheme I) was proposed[9] to react with another aldehyde molecule to give acyl–alkoxo-type intermediate **4**. Reductive elimination of ester from **4** would lead to regeneration of the catalytically active ruthenium(0) species [L_3Ru].

$$\underset{\mathbf{3}}{\mathrm{ArCORu(H)L_3}} + \mathrm{ArCHO} \rightarrow \underset{\mathbf{4}}{\mathrm{ArCORu(OCH_2Ar)L_3}} \rightarrow \mathrm{ArCOOCH_2Ar} + [\mathrm{L_3Ru}]$$

A possible mechanism for the rhodium-catalyzed homogeneous Rosenmund-type reaction is probably the same as that for the hydrogenolysis of the carbon–chlorine bond in chloroarenes catalyzed by the same complex under phase-transfer or biphasic conditions.[12]

In conclusion, this research has resulted in the first examples of metal complex catalyzed homogeneous Rosenmund-type reduction and of a one-pot Rosenmund reduction and Tishchenko disproportionation reactions of acid chlorides.

Experimental Section

Spectral measurements were carried out on the following equipment: Varian XL 300 (^{1}H NMR), Bomemn MB-100 (FT-IR), and VG 5050 micromass (mass spectra) spectrometers. Melting points were determined with a Fisher-Johns apparatus. A Varian 6000 instrument was used for GLC analysis, using 3% OV-17 on Chromosorb W. Benzoyl chloride (Fisher Scientific Company) was distilled under reduced pressure prior to use. All other acid chlorides, triethylamine, 2,4,6-collidine, and triphenylphosphine were purchased from Aldrich Chemical Co. and were used as received, as were aqueous ruthenium trichloride (Johnson-Matthey) and hydrogen (Air Products). The complexes [$(Cy_3P)_2Rh(H)Cl_2$],[12] [$(Ph_3P_3)Ru(H)Cl$] (the aqueous $NaBH_4/C_6H_6$ procedure of Wilkinson and co-workers was used),[14] and [$(Ph_3P)_3RuCl_2$][22] were prepared as described in the literature.

2-Napthaldehyde from 2-Naphthoyl Chloride. A mixture of 2-naphthoyl chloride (0.29 g, 1.52 mmol), benzene (2 mL), triethylamine (1.1 mL), and [$(Cy_3P)_2Rh(H)Cl_2$] (0.075 g, 0.1 mmol) was placed in a 150-mL Schlenk tube, and the mixture was immediately degassed by two freeze–pump–thaw cycles. The Schlenk tube was purged with H_2, and the reaction mixture was vigorously stirred under H_2 at 50 °C (oil bath) for 65 h. Water (10 mL) and benzene (12 mL) were added, and the organic layer was separated, washed with water (2 × 10 mL), and subjected to rotary evaporation. The residue was chromatographed on silica gel first with pentane, to give naphthalene (0.006 g; 3.5%), mp 80–82 °C, and then with benzene, to form 0.242 g of crude 2-naphthaldehyde. The latter was purified by vacuum sublimation: yield 0.145 g (61%); mp 60–62 °C (lit.[23] mp 59–62 °C). ^{1}H NMR: δ 7.5–8.4 (m, 7 H, $C_{10}H_7$), 10.1 (s, 1 H, CHO).

The reaction of benzoyl chloride under the same conditions afforded benzaldehyde in 30% yield (GLC using internal standard).

General Procedure for the Ruthenium-Catalyzed Preparation of Esters from Acid Chlorides. A solution of toluene (2 mL), acid chloride (1 mmol), and 2,4,6-collidine (2 mmol) was placed in a 150-mL Schlenk tube. The ruthenium complex (0.05 mmol; see Table I) was added to the degassed solution, and the mixture was immediately degassed by two freeze–pump–thaw cycles. The Schlenk tube was purged with H_2, and the reaction mixture was stirred under H_2 at 55 °C (oil bath; see Table I for reaction times). Benzene (10 mL) was added, the mixture was washed with 10% HCl (2 × 5 mL), and the organic extract was concentrated by rotary evaporation. The residue was chromatographed on silica gel to give the pure ester. For C_6H_5COCl, $CH_3C_6H_4COCl$, and $CH_3OC_6H_4COCl$, the residue was dissolved in pentane, the solution was filtered through a short silica plug, and the filtrate was concentrated by rotary evaporation and dried.

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Optically Pure 1,3-Diols from (2*R*,4*R*)- and (2*S*,4*S*)-1,2:4,5-Diepoxypentane

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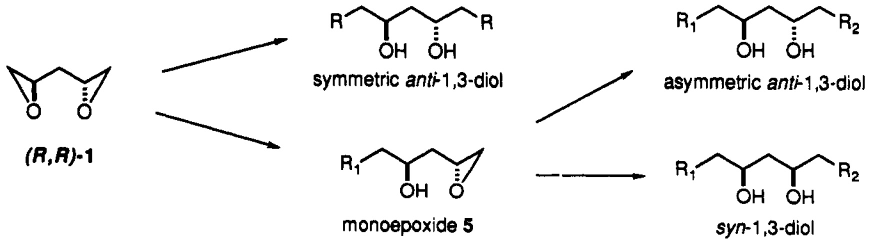
Optically pure (>97% ee) (2*R*,4*R*)-1,2:4,5-diepoxypentane (**1**) and its enantiomer can be prepared in three steps from 2,4-pentanedione without the need for chromatographic purification. Diepoxide **1** is an efficient precursor to a wide variety of optically pure syn and anti 1,3-diols. Reaction with excess nucleophile gives symmetric anti 1,3-diols in good yield. Reaction with a slight excess of alkyllithium under Ganem's conditions gives the monoepoxides **5** in good yield. Addition of a second nucleophile to monoepoxide **5** gives asymmetric anti 1,3-diols. Mitsunobu inversion of monoepoxide **5** followed by addition of a second nucleophile gives syn 1,3-diols. Optically pure syn and anti 1,3-diols are available from diepoxide **1** in one to three steps and good overall yield.



We became interested in the C_2 symmetric diepoxide **1** as a building block for 1,3-diols as part of a convergent strategy to prepare alternating polyol chains of the type found in polyene macrolide antibiotics. Our initial syn-

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