Alkylation of Acid Chlorides by Alkylrhodium(I) Complexes

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Abstract: The alkylation of acid chlorides by alkylrhodium(I) complexes to produce ketones is reported in full detail. Thus alkyl, aryl, vinyl, and α-chloro acid chlorides are converted to the corresponding methyl, *n*-butyl, phenyl, and allyl ketones in moderate to high yield. This method is used to convert (*S*)-(+)-2-methylpentanoyl chloride to (*S*)-(+)-4-methyl-3-heptanone (the principal alarm pheremone of fungus-growing ants of the genus *Atta*) without racemization of the chiral center. Alkylrhodium(I) complexes react specifically with acid chlorides and are inert toward aldehydes, esters, amides, nitriles, and other organic halides. The process is thought to occur via oxidative addition–reductive elimination sequences, which regenerate the initial rhodium complex in the last step.

Alkyl- and arylrhodium(I) complexes have been prepared by the action of Grignard or organolithium reagents on the corresponding chlororhodium(I) complexes.[1] Their mode of decomposition[1,2] and their reactions with alkenes, alkynes,[3] and aryl halides[4] have recently been reported. A preliminary report from our laboratories[5] detailed a general ketone synthesis (Scheme I) based on the oxidative addition of acid chlorides to alkyl- and arylrhodium(I) complexes. This paper presents the full details of this study.

Results and Discussion

The general reaction, as well as the most likely mechanism for the transformation, is detailed in Scheme I. Thus a THF suspension of the readily available[6] chloro(carbonyl)bis(triphenylphosphine)rhodium(I) complex (**1**) is treated with the appropriate Grignard or organolithium reagent at low temperature producing within 0.5 hr a solution of the orange-to-red alkylrhodium(I) complex (**2**). The desired acid chloride is added and, over a course of hours, yellow crystals of the starting complex (**1**) precipitate. After warming to 25°, hexane is added to complete precipitation of the inorganics, and the resulting slurry is filtered. The filtrate contains the product ketone, which is purified by standard methods. Pure starting complex (**1**) is recovered in high yield by dissolution of the precipitate in chloroform followed by precipitation of the rhodium complex by addition of methanol. Material recovered in this fashion is of sufficient quality for reuse in Scheme I.[7] Thus, this conversion of acid halides to ketones ensues with *no net consumption* of rhodium complex (**1**).

Table I lists the various ketones prepared by this method. Aryl and primary alkyllithium or Grignard reagents lead to the corresponding ketones in high yield. α-Chloroacetyl chloride reacts *exclusively* at the acyl halide, producing α-chloro ketones in good yield. (*S*)-(+)-4-Methyl-3-heptanone has been identified[8] as the principal alarm pheremone of fungus-growing ants of the genus *Atta*. Enantiomerically enriched (*S*)-(+)-2-methylpentanoic acid, prepared by the method of Meyers,[9] was converted (via the acid chloride) to (*S*)-(+)-4-methyl-3-heptanone with *no* racemization of the chiral center. This sequence provides an efficient asymmetric total synthesis of the pheremone and illustrates the utility of the rhodium reaction for the preparation of sensitive compounds.

With allylmagnesium bromide, the β,γ-unsaturated ketones from lauroyl chloride and benzoyl chloride could be obtained without isomerization to the more stable α,β-unsaturated isomer. With cinnamoyl chloride, mixtures of α,β- and β,γ-unsaturated ketones were obtained.[10]

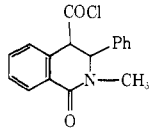
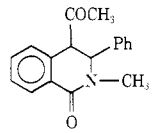
With secondary or tertiary organolithium reagents, the reaction depicted in Scheme I leads to very low yields of ketone. A careful examination of the reaction mixture from *sec*-butyllithium, the chlororhodium(I) complex, and benzoyl chloride revealed only 3% of the desired *sec*-butyl ketone, as well as 9% of the corresponding *n*-butyl ketone. The remainder of the organic material was unreacted benzoyl chloride. This is likely due to facile decomposition of secondary and tertiary alkylrhodium(I) complexes via β-hydride abstraction (vide infra), limiting this method to the use of primary alkylrhodium complexes. Stabilized carbanions such as cyanomethyllithium and nitromethyllithium[11] also fail to produce significant amounts of ketone by this sequence.

The alkylation reaction depicted in Scheme I is specific for acid chlorides. Aldehydes, esters, and nitriles are unreactive as evidenced by the quantitative recovery of benzaldehyde, ethyl benzoate, and benzonitrile added concurrently with the acid chloride and carried through the normal reaction and isolation procedures. Alkyl halides were also generally inert to the reaction conditions. Prolonged reaction of methyl iodide with the phenylrhodium I complex (**2**) led to a very low yield of acetophenone (from CO insertion), while higher iodides and other simple halides did not react under conditions sufficiently severe to decompose the rhodium complex. Even the normally highly reactive α-chloroketones are inert to the alkylrhodium(I) complexes, as evidenced by the clean conversion of chloroacetyl chloride to the corresponding α-chloro ketone in high yield.

Mechanistic Considerations

The proposed mechanism (Scheme I) for this reaction involves conversion of the chlororhodium(I) complex (**1**) to an alkylrhodium(I) species (**2**), oxidative addition of acid halide to produce the alkylacylrhodium(III) complex (**3**), and reductive elimination of ketone with concomitant regeneration of the initial chlororhodium(I) complex (**1**). Although these alkylrhodium(I) and alkylacylrhodium(III) complexes have not been isolated and characterized, there is ample precedent for their existence and their role in this reaction sequence. The reaction of organolithium or Grignard reagents and halorhodium(I) complexes to produce alkylrhodium(I) complexes (**1** → **2**) is well established.[1,3,4] The iridium analog of **2** synthesized by this method has recently been isolated and characterized,[12] as has a vinylrhodium(I) analog of **2** (R = MeOOCCH=C(COOMe)-).[2] All of our attempts to isolate the phenyl and methylrhodium(I) complexes (**2**, R = Ph, CH_3) led to pale yellow solids which rapidly darkened as solvent was removed and led to impure

Table I. Reaction of Alkylrhodium(I) Complexes with Acid Chlorides

Acid chloride	RM	Product[a]	Yield, %[b]
n-$C_{11}H_{23}COCl$	CH_3Li	n-$C_{11}H_{23}COCH_3$	77
	CH_3MgI		58
	n-C_4H_9Li	n-$C_{11}H_{23}CO(CH_2)_3CH_3$	80
	C_6H_5Li	n-$C_{11}H_{23}COC_6H_5$	96
	C_6H_5MgBr		85
	CH_2=$CHCH_2MgBr$	n-$C_{11}H_{23}COCH_2CH$=CH_2	83
C_6H_5COCl[c]	CH_3Li	$C_6H_5COCH_3$	82
	n-C_4H_9Li	$C_6H_5CO(CH_2)_3CH_3$	74
	C_6H_5Li	$C_6H_5COC_6H_5$	94
	CH_2=$CHCH_2MgBr$	$C_6H_5COCH_2CH$=CH_2	71
trans-$C_6H_5CHCHCOCl$	CH_3Li	*trans*-C_6H_5CH=$CHCOCH_3$	68
	n-C_4H_9Li	*trans*-C_6H_5CH=$CHCO(CH_2)_3CH_3$	68
	C_6H_5Li	*trans*-C_6H_5CH=$CHCOC_6H_5$	85
	C_6H_5MgBr		58
	CH_2=$CHCH_2MgBr$	*trans*-C_6H_5CH=$CHCOCH$=$CHCH_3$	80
CH_3COCl	C_6H_5Li	$C_6H_5COCH_3$	65
$ClCH_2COCl$	n-C_4H_9Li	$ClCH_2CO(CH_2)_3CH_3$	55
	C_6H_5Li	$ClCH_2COC_6H_5$	80
$C_2H_5CH(CH_3)COCl$	C_6H_5Li	$C_2H_5CH(CH_3)COC_6H_5$	69
(S)-(+)-$C_3H_7CH(CH_3)COCl$	C_2H_5Li	(S)-(+)-$C_3H_7CH(CH_3)COC_2H_5$	83[d]
n-$C_6H_{13}CH(CH_3)CH_2COCl$	CH_3Li	n-$C_6H_{13}CH(CH_3)CH_2COCH_3$	81
	CH_3Li		55
C_6H_5COCl	$C_2H_5CH(CH_3)Li$	$C_2H_5CH(CH_3)COC_6H_5$	3
		$CH_3(CH_2)_3COC_6H_5$	9

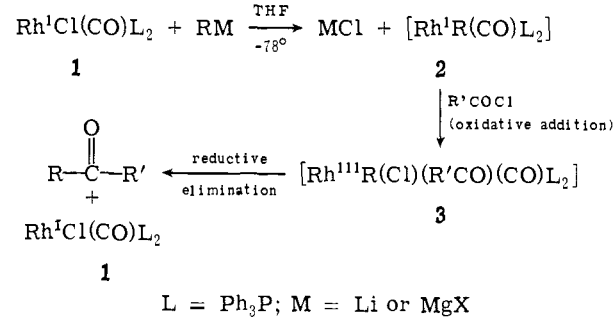
[a] Identified by infrared, NMR, mass spectra, and comparison with authentic material. All new compounds gave satisfactory elemental analysis. [b] Yield of isolated product, purified by column or preparative layer chromatography. [c] Excess (10%) alkylrhodium must be used to ensure complete conversion with this substrate. [d] This reaction proceeded with *complete retention* of stereochemistry.

and uncharacterized solids. However, these complexes appear to be somewhat more stable in THF solution, and infrared spectra of the homogeneous solutions resulting from treatment of **1** with methyl or phenyllithium had CO absorptions at 1962 and 1969 cm^{-1}, respectively, indicative of alkylrhodium(I) species. (The CO band of $RhCl(CO)(PPh_3)_2$ appears at 1980 cm^{-1} under these conditions.)

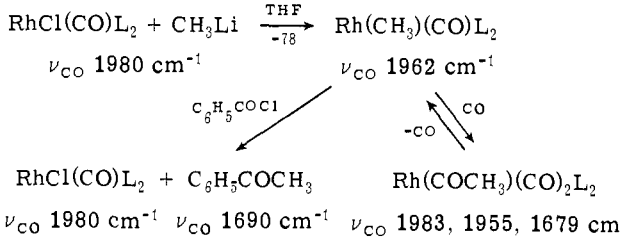
A portion of the $Rh(CH_3)(CO)(PPh_3)_2$ solution was stirred for 1 hr under an atmosphere of CO (Scheme II). The color of the solution went from red to pale yellow, and the solution developed infrared bands at 1983 and 1955 cm^{-1} (Rh(I)CO) as well as a band at 1679 cm^{-1} ($RhCOCH_3$). This complex is inferred to be $Rh(COCH_3)(CO)_2(PPh_3)_2$,[13] resulting from carbonylation and insertion of CO by $Rh(CH_3)(CO)(PPh_3)_2$. This complex readily lost CO, regenerating the alkylrhodium(I) complex.

The oxidative addition of acid chlorides to coordinatively unsaturated metal(I) complexes to produce acylmetal(III) complexes (**2** → **3**) is also well established. The enhanced reactivity of acid halides with **2** (hours at −78°) compared with **1** (inert)[14] is likely a result of the increased electron density at the central metal caused by replacement of halogen with alkyl.[15] All attempts to even detect complex **3** failed. Addition of benzoyl chloride to a THF solution of **2** (R = Me) resulted in a solution with infrared adsorptions at 1980 (ν_{CO} $RhCl(CO)(PPh_3)_2$), 1962 (ν_{CO} $Rh(CH_3)(CO)(PPh_3)_2$), 1794 and 1734 (ν_{CO} PhCOCl), and 1690 cm^{-1} (ν_{CO} $PhCOCH_3$). There were *no* absorptions in the 2100–2000 cm^{-1} region, indicating the absence of acylrhodium species (Scheme II). Thus the Rh^{III} (alkyl)(acyl) complex **3** must be very unstable and collapse immediately to ketone and starting complex **1**. As the reaction progressed, the band at 1962 cm^{-1} decreased and the band at 1980 cm^{-1} increased as $Rh(CH_3)(CO)(PPh_3)_2$ was converted to $RhCl(CO)(PPh_3)_2$. A similar series of reactions

Scheme I



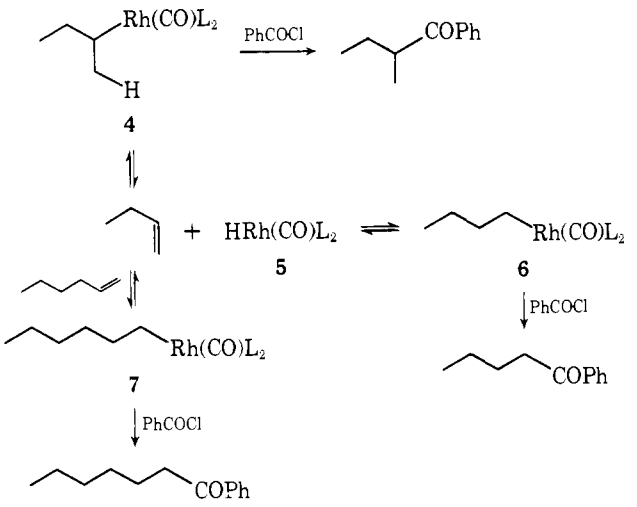
Scheme II



was carried out using phenyllithium and acetyl chloride in THF at −78°. Again no Rh^{III}(acyl)(alkyl) complex was detected.

The observation that secondary and tertiary alkylrhodium(I) complexes lead to very low yields of ketones and that the *sec*-butylrhodium(I) complex upon treatment with benzoyl chloride produced a mixture of ketones in which the *n*-butyl ketone predominated over the *sec*-butyl ketone by a factor of 3:1 is rationalized by a facile β-hydride elimination.[17] The equilibria involved in this process are depicted in

Scheme III



Scheme III. β-hydride abstraction in the initially formed secondary alkylrhodium(I) complex (**4**) would produce 1-butene and a hydridorhodium(I) complex (**5**). Since this equilibrium is likely to lie to the rhodium hydride–olefin side[18] the low yield of ketone is explained by loss of alkylrhodium(I) complex by this route. However, readdition occurs to a small extent, with the metal atom bonding preferentially to the primary position,[19] producing the *n*-butyl complex **6** and ultimately the observed *n*-butyl ketone. Additional evidence for the intermediacy of a hydridorhodium species in these reactions was obtained by successive treatment of $RhCl(CO)L_2$ with *tert*-butyllithium and benzoyl chloride in the presence of a large excess of 1-hexene. The sole ketonic product was 1-phenyl-1-heptanone (13%), resulting from interception of the rhodium hydride by 1-hexene.[20]

Conclusions

A large number of new methods for the conversion of acid halides to ketones, including several based on transition metal intermediates, have been reported in the last few years,[21] and comparison with the method reported herein is useful. This rhodium-based method has several limitations. It is restricted to use with primary alkyl, aryl, or allyllithium or Grignard reagents, thereby limiting the types of ketones available by this method. Despite the fact that the starting rhodium complex is *not* consumed during the reaction but is regenerated in the last step, the high initial cost of the rhodium complex[6] makes this route unappealing for routine conversions in simple systems, and one of the several alternative procedures available should be used. However, this rhodium-based method is probably the mildest, most specific, and most tolerant of functionality of the currently available methods. It is technically easy to carry out, proceeds in high yield, and leads to products that are easily purified. For sensitive systems requiring these features, it warrants consideration.

Experimental Section

General. All melting points are uncorrected. Infrared spectra were measured with either Perkin-Elmer Models 337 or 267 spectrophotometers. Nuclear magnetic resonance spectra were measured with either Varian Models A60A or T60 spectrometers. Gas chromatography was performed using a Bendix Model 2300 gas chromatograph equipped with either a 10 ft × 0.25 in. 10% SE-30–Chromosorb W column (column A) or a 10 ft × 0.25 in. 4% Carbowax 20 M–Chromosorb G-AW column (column B). Silica gel column chromatography was performed using Baker reagent silica gel 60–200 mesh. Layer chromatography was performed using Brinkmann silica gel PF254 analytical and preparative plates, visualized by uv light. Microanalyses were performed by Midwest Microanalytical Laboratory, Indianapolis, Ind. All reactions involving alkyl- and arylrhodium complexes were carried out under an argon atmosphere in three-necked flasks of suitable size, equipped with serum caps (or dropping funnels for large scale runs). Reagents were added using gas-tight syringes. All compounds had infrared, NMR, and mass spectra consistent with the proposed structure. Known compounds were further characterized by preparation of derivatives or by melting points and in many cases by comparison with authentic material. All new compounds had acceptable elemental analyses.

Materials. Tetrahydrofuran was distilled from lithium aluminum hydride under nitrogen and flushed with argon prior to use. Ether (Fisher anhydrous reagent grade) was used without further purification. Hexane (Fisher reagent grade) was redistilled prior to use. Acid chlorides were either purchased commercially or prepared from the acids by standard methods; all acid chlorides were redistilled prior to use. Phenylmagnesium bromide was prepared by standard methods. Allylmagnesium bromide was prepared by the method described in ref 22, filtered, and stored under argon. Other Grignard or organolithium reagents were purchased commerically. All Grignard and organolithium reagents were titrated prior to use.[23]

General Procedure for the Alkylation of Acid Halides by Alkylrhodium(I) Complexes. Preparation of 2-Tridecanone. A suspension of chloro(carbonyl)bis(triphenylphosphine)rhodium(I) (**1**) (6.91 g, 10 mmol) in THF (75 ml) was thoroughly degassed and cooled to −78° with vigorous stirring. Methyllithium (4.7 ml of a 2.13 *M* solution in ether, 10 mmol) was added via dropping funnel and the resulting mixture stirred for 1 hr. Then lauroyl chloride (2.19 g, 10 mmol) was added via syringe; the mixture was stirred at −78° for several hours and gradually allowed to warm to room temperature. It was then diluted with 100 ml of hexane,[24] cooled to 0° for several hours (to ensure complete precipitation of the rhodium complex), filtered, and washed with hexane. The filtrate was evaporated to dryness and the residue purified by silica gel column chromatography to remove traces of the rhodium complex. Elution with 5:1 pentane–ether yielded 1.52 g (77%) of the desired product **4**; a yellow (2,4-dinitrophenyl)hydrazone was prepared, mp 69–70° (reported[25] 69°).

5-Hexadecanone. This compound was prepared in 80% yield from *n*-butyllithium and lauroyl chloride by the above method and purified by silica gel column chromatography (eluted with 6:1 hexane–ether), mp 32–34° (collected from the gas chromatograph, column B, 205°, 6.9 min) (reported[26] 37–38.5°).

Laurophenone. This compound was prepared in 96% yield from phenyllithium and lauroyl chloride by the above method and purified by silica gel column chromatography (eluted with 6:1 hexane–ether), mp 43–45° (after recrystallization from ethyl acetate–hexane) (reported[27] 46–47°).

1-Pentadecen-4-one. This compound was prepared in 83% yield from allylmagnesium bromide and lauroyl chloride by the above method and purified by column chromatography on Florisil[28] (eluted with 1:1 hexane–ether): mp 48–52° (unrecrystallized); ir (melt) 1710, 1640 cm^{-1}; NMR ($CDCl_3$) δ 0.90 (t, 3 H), 1.30 (s, 18 H), 2.40 (m, 2 H), 3.16 (d, 2 H), 5.05 (d, 1 H), 5.30 (s, 1 H), 5.65–6.25 (m, 1 H).

Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.22; H, 12.36.

Acetophenone. This compound was prepared in 82% yield from methyllithium and benzoyl chloride by the above method.[29] After purification by preparative layer chromatography (developed with 5:1 hexane–ether), it was identical in all respects with authentic material.

Valerophenone. This compound was prepared in 74% yield from *n*-butyllithium and benzoyl chloride by the above method.[29] After purification by silica gel column chromatography (eluted with 9:1 hexane–ether), it was identical in all respects with authentic material.

Benzophenone. This material was prepared in 94% yield from phenyllithium and benzoyl chloride by the above method.[29] After purification by silica gel column chromatography (eluted with 10:1 hexane–ether), it was identical in all respects with authentic material.

3-Butenophenone. This material was prepared in 71% yield from allylmagnesium bromide and benzoyl chloride by the above method and purified by column chromatography on Florisil[28] (eluted with 1:1 hexane-ether); ir (neat) 1690, 1665, 1600, 1580 cm^{-1}; NMR ($CDCl_3$) 3.74 (d, 2 H), 5.16 (m, 1 H), 5.40 (s, 1 H), 5.85-6.50 (m, 1 H), 7.15-8.15 (m, 5 H).

Anal. Calcd for $C_{10}H_{10}O$: C, 82.16; H, 6.89. Found: C, 81.94; H, 7.06.

Benzalacetone. This material was prepared in 68% yield from methyllithium and cinnamoyl chloride[30] by the above method. After purification by silica gel column chromatography (eluted with 9:1 hexane-ether), it was identical in all respects with authentic material.

1-Phenyl-1-hepten-3-one. This material was prepared in 68% yield from *n*-butyllithium and cinnamoyl chloride[30] by the above method and purified by preparative layer chromatography (developed twice with 5:1 hexane-ether); a red (2,4-dinitrophenyl)hydrazone was prepared, mp 197-200° (reported[31] 200°).

Chalcone. This material was prepared in 85% yield from phenyllithium and cinnamoyl chloride[30] by the above method. After purification by silica gel column chromatography (eluted with 10:1 hexane-ether), it was identical in all respects with authentic material.

1-Phenyl-1,4-hexadien-3-one. This material was isolated[10] in 80% yield from the reaction of allylmagnesium bromide and cinnamoyl chloride[30] by the above method and purified by column chromatography on Florisil (eluted with 1:1 hexane-ether); a red (2,4-dinitrophenyl)hydrazone was prepared, mp 182-185° (reported[32] 185°).

1-Chloro-2-hexanone. This material was prepared in 55% yield from *n*-butyllithium and chloroacetyl chloride by the above method and purified by preparative layer chromatography (developed with 3:1 hexane-ether): ir (neat) 1710 cm^{-1}; NMR ($CDCl_3$) 0.95 (t, 3 H), 1.5 (m, 4 H), 2.6 (t, 2 H), 4.1 (s, 2 H).

Anal. Calcd for $C_6H_{11}ClO$: C, 53.54; H, 8.24; Cl, 26.34. Found: C, 53.78; H, 8.34; Cl, 26.17.

Phenacyl Chloride. This material was prepared in 80% yield from phenyllithium and chloroacetyl chloride by the above method. After purification by preparative layer chromatography (developed with 4:1 hexane-ether), it was identical in all respects with authentic material.

2-Methylbutyrophenone. This material was prepared in 69% yield from phenyllithium and 2-methylbutyryl chloride[33] by the above method and purified by preparative layer chromatography (developed twice with 2:1 hexane-ether); a yellow (2,4-dinitrophenyl)hydrazone was prepared, mp 127-129° (reported[34] 127-128°).

(*S*)-(+)-2-Methylpentanoic Acid. This material was prepared in 71% yield by the method of Meyers,[9] $[\alpha]^{24}D$ +13.9° (neat), 76% enantiomeric excess.[35] The specific rotation of this material as measured in either a 1 or 10% solution in chloroform was identical with the specific rotation observed for the neat liquid.

(*S*)-(+)-Methyl-3-heptanone. This material was prepared in 83% yield from ethyllithium and (*S*)-(+)-2-methylpentanoyl chloride by the above method and purified by column chromatography on Florisil[36] (eluted with 5:1 pentane-ether), $[\alpha]^{24}D$ +16.8° (*c* 4.26, hexane), 76% enantiomeric excess. This material was identical in all respects including rotation with material prepared by the method of Silverstein,[8] from 76% optically pure acid.

4-Methyl-2-decanone. This material was prepared in 81% yield from methyllithium and 3-methylnonanoyl chloride[37] by the above method and purified by column chromatography on Florisil (eluted with 5:1 hexane-ether). Material obtained in this manner was identical in all respects with that prepared by a different method.[38]

***N*-Methyl-1-oxo-1,2,3,4-tetrahydro-3-phenyl-4-acetylisoquinoline.** This material was prepared in 55% yield from methyllithium and *N*-methyl-1-oxo-1,2,3,4-tetrahydro-3-phenyl-4-chloroformylisoquinoline by the above method and purified by preparative layer chromatography (developed once with ether and twice with 1:1 hexane-ether): mp 130-132° (after recrystallization from hexane); ir ($CHCl_3$) 1705, 1600, 1575 cm^{-1}; NMR ($CDCl_3$) 2.10 (s, 3 H), 3.10 (s, 3 H), 3.75 (d, J = 2 Hz, 1 H), 5.28 (d, J = 2 Hz, 1 H), 7.30-8.20 (m, 9 H).

Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.23; H, 5.94; N, 4.81.

Reaction of *sec*-Butyllithium with Phenylrhodium Complex 2 (R = C_6H_5). Chloro(carbonyl)bis(triphenylphosphine)rhodium(I) (691 mg, 1 mmol) was suspended in 20 ml of THF, degassed, cooled to −78°, and treated sequentially with *sec*-butyllithium (0.64 ml of a 1.56 *M* solution, 1 mmol) and benzoyl chloride (0.116 ml, 1 mmol) according to the procedure described above. The crude product mixture (which consisted primarily of unreacted benzoyl chloride) was separated by preparative layer chromatography (developed three times with 2:1 hexane-ether). A 3:1 mixture of two ketones was obtained, 20 mg (12% yield). The major and minor ketonic products were identified as valerophenone and 2-methylbutyrophenone, respectively, by GC coinjection (column A) with samples of authentic material.

1-Phenyl-1-heptanone. Chloro(carbonyl)bis(triphenylphosphine)rhodium(I) (500 mg, 0.73 mmol), and 1-hexene (614 mg, 7.3 mmol) were suspended in 15 ml of THF, degassed, cooled to −78°, and treated sequentially with *tert*-butyllithium (0.536 ml of a 1.36 *M* solution, 0.73 mmol) and benzoyl chloride (0.085 ml, 0.73 mmol) according to the procedure described above. The crude product mixture (which consisted primarily of unreacted benzoyl chloride) was separated by preparative layer chromatography (developed with 3:1 hexane-ether). A single ketone was obtained, 18 mg (13% yield); this was identified as 1-phenyl-1-heptanone from its infrared, NMR, and mass spectra.

Infrared Studies of Methylrhodium Complex 2 (R = CH_3). This complex was prepared from complex **1** and methyllithium by the method described above. One hour after the addition of the methyllithium, an aliquot of the reaction mixture was withdrawn via syringe and placed in a sealed AgBr cell which had been flushed with argon. A band was observed at 1962 cm^{-1}. A portion of the solution was transferred to another precooled flask and treated with benzoyl chloride. After 2 hr, an aliquot was withdrawn and exhibited bands at 1980, 1962, 1794, 1734, and 1690 cm^{-1}. Aliquots were examined periodically; the bands at 1962, 1794, and 1734 cm^{-1} gradually decreased in intensity, and the bands at 1980 and 1690 cm^{-1} increased. The remaining portion of the original solution of **2** (R = CH_3) was opened to a balloon filled with CO; after stirring for 0.5 hr at −78°, it had turned greenish yellow. An aliquot was withdrawn and exhibited infrared absorptions at 1983, 1955, and 1679 cm^{-1}.

Infrared Studies of Phenylrhodium Complex 2 (R = Ph). This complex was prepared from **1** and phenyllithium, as described above; it exhibited an infrared band at 1969 cm^{-1}. After treatment with acetyl chloride, it exhibited bands at 1980, 1969, 1772, and 1690 cm^{-1}. The bands at 1980 and 1690 cm^{-1} gradually increased and the bands at 1969 and 1772 cm^{-1} gradually decreased as the reaction progressed. Treatment with CO for 0.5 hr gave a greenish-yellow solution which exhibited bands at 1983, 1938, and 1664 cm^{-1}.

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One-Electron vs. Two-Electron Oxidations. Vanadium(V) Oxidation of Cyclobutanols[1]

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Abstract: Vanadium(V) in aqueous perchloric acid oxidized 2-ethylcyclobutanols and 2,2-dimethylcyclobutanol to 4-hydroxyhexanal and 4-hydroxy-4-methylpentanal, respectively. In $H_2{}^{18}O$ cyclobutanol gives 4-hydroxybutanol with ^{18}O incorporated in the hydroxyl group. The oxidation of the cyclobutanols follows the rate law $v = k[V(V)][ROH]h_0$, with the relative reactivities for cyclobutanol, 2-ethylcyclobutanol, and 2,2-dimethylcyclobutanol being 1.0, 6.6, and 147; *cis*- and *trans*-2-ethylcyclobutanol are equally reactive. Methyl cyclobutyl ether is 10^4 times less reactive than cyclobutanol. The results are consistent with a mechanism in which the rate limiting step is the carbon–carbon bond cleavage in a cyclobutyl ester intermediate, $C_4H_7OVO^{2+}$(aq), leading to an acyclic free radical, $\cdot CR_2CH_2CH_2CHO$, which is subsequently oxidized to the hydroxy aldehyde. Methyl cyclohexyl ether is also found to be unreactive toward vanadium(V) oxidation; this suggests that the ester mechanism is generally applicable to vanadium(V) oxidations of alcohols.

Cyclobutanol exhibits the unique property of reacting in basically different ways with one-electron and two-electron oxidants. Chromium(VI) and chromium(V), which are known to react preferably as two-electron oxidants, oxidize cyclobutanol to cyclobutanone with the carbon–hydrogen cleavage occurring in the rate-limiting step.[2,3] A large isotope effect (k_H/k_D = 9.3), observed in a preliminary exploration of the permanganate oxidation of cyclobutanol,[4] indicates a similar course for the manganese(VII) oxidation.

With one-electron oxidants cyclobutanol reacts preferentially with carbon–carbon bond cleavage resulting in the opening of the cyclobutane ring. Chromium(IV) oxidation in aqueous solutions leads to the formation of γ-hydroxybutyraldehyde.[2,3] The same product is formed in the chromic acid oxidation in the presence of large amounts of manganese(II) under conditions where manganese(III) appears to be the actual oxidant.[5] Similarly, cerium(IV) oxidation gives only ring cleavage products formed through the free radical $\cdot CH_2CH_2CH_2CHO$.[6] Predominantly ring cleavage products were also obtained in the oxidation of cyclobutanol by lead tetraacetate[7] and of 1-methylcyclobutanol with iron(III) chloride.[8,9]

Despite its common occurrence in one-electron oxidations, the mechanism of the oxidation of cyclobutanols to γ-hydroxyaldehydes was not well understood; more detailed investigation of the reaction was hampered by the fact that in none of the above examples did the reaction occur alone. A further study of the reaction has now become possible due to the finding that vanadium(V)[12] reacts with cyclobutanol to give γ-hydroxybutyraldehyde in almost quantitative yields.[5]

The main questions to which we were seeking answers were the following. (1) Does the oxidation of cyclobutanol proceed through a free radical intermediate? (2) What is the effect of β-substitution on the direction of cleavage and on the rate of the reaction? (3) How important is the contribution of nonbonded interactions in determining the reactivity of cyclobutanols and their preference for ring cleavage? (4) Could the formation of the cleavage product be explained by a mechanism involving ring expansion to an oxy-