

PALLADIUM-CATALYSED OXIDATION OF ALCOHOLS WITH CARBON TETRACHLORIDE, FORMATION OF 4,4,4-TRICHLORO KETONES FROM ALLYLIC ALCOHOLS AND CARBON TETRACHLORIDE OR BROMOTRICHLOROMETHANE, AND CONVERSION OF HALOHYDRINS TO KETONES

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Abstract—Pd salts catalyse oxidation of alcohols with CCl₄ in the presence of K₂CO₃. Primary alcohols are oxidised to esters, and secondary alcohols to ketones. CCl₄ is converted to CHCl₃. The reaction of allylic alcohols bearing a terminal olefinic bond with CCl₄ or BrCCl₃ in the presence of palladium catalyst at 110° affords 4,4,4-trichloro ketones. At 40°, simple adducts of CCl₄ or BrCCl₃ having a halohydrin structure are obtained, which are converted to the corresponding trichloro ketones by the catalysis of palladium. Various halohydrins are converted to ketones by Pd catalysis.

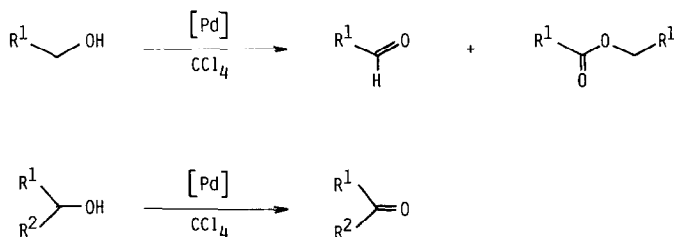
In our continuing effort to study the Pd-catalysed reactions of polyhaloalkanes, our main interest has been to compare the reactivities of polyhaloalkanes with those of aryl and alkenyl halides in the presence of Pd catalysts. Their reactivities are clearly different in reactions involving olefins.^{1–3} But we have found some similarities in the reactions involving alcohols. We have found that by the catalysis of Pd, secondary alcohols are oxidised to ketones with CCl₄ which is converted to CHCl₃.⁴ Primary alcohols are oxidised to esters under the same conditions. This reaction can be compared with the Pd-catalysed oxidation reaction of alcohols with aryl halides reported by Tamaru *et al.*^{5–7} Also we have found that the Pd-catalysed reaction of allylic alcohols with CCl₄ and BrCCl₃ is neither a simple addition of CCl₄ and BrCCl₃ to olefinic bonds, nor oxidation of the OH group. In this reaction introduction of a trichloromethyl group and oxidation of the OH group take place concomitantly to afford

conversion of various halohydrins to ketones with Pd catalysts.¹¹ Preliminary reports on these reactions have been given,^{4,8,11} and details of the reactions are presented in this paper.

RESULTS AND DISCUSSION

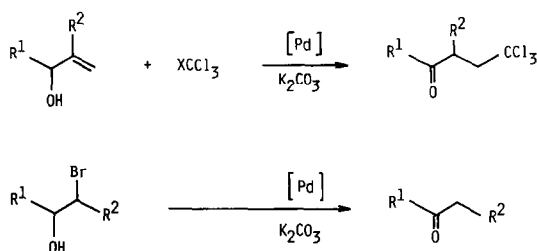
1. Oxidation of alcohols⁴

It is known that Pd(II) salts in alcoholic media are reduced to Pd(0) accompanied by dehydrogenation of the OH group. In order to recycle the Pd, various oxidants of Pd(0) such as Cu salts¹² and aryl halides^{5–7} are used. We have found that Pd salts catalyse the oxidation of alcohols with CCl₄ in the presence of excess K₂CO₃, in which CCl₄ is considered to be a novel oxidant of Pd(0). Several Pd salts such as PdCl₂ and Pd(OAc)₂ are active for the oxidation in the presence or absence of phosphines. Typical examples of the oxidation catalysed by PdCl₂ are shown in Table 1.



Scheme 1.


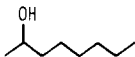
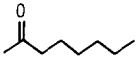




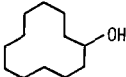
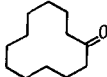
4,4,4-trichloro ketones.⁸ This reaction is closely related to the well-known reactions of aryl and alkenyl halides with allylic alcohols to form β-aryl and alkenyl ketones reported by Chalk and Magennis⁹ and Melpolder and Heck.¹⁰ In our reaction, polyhaloalkanes add to the olefinic bond of allylic alcohols to form halohydrins, which are converted to ketones by the catalysis of Pd. As an extension of this reaction, we have carried out the



Scheme 2.

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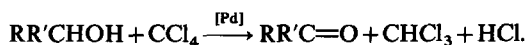
Table 1. Oxidation of alcohols with PdCl₂/CCl₄/K₂CO₃ system^a

Entry	Alcohols	Cat. (%)	Temp. (°)	Time (hr)	Products	Yields (%)
1		1	80	24	C ₈ H ₁₇ OCOC ₇ H ₁₅	73
2	PhCH ₂ OH	2	80	7	PhCHO (57) PhCO ₂ CH ₂ Ph (35) PhCH ₂ OCH ₂ Ph (8)	70
3		1	80	24		65
4		2	80	72		63
5		2 1	80 120	24 24		55 75
6		2 1	80 120	72 24		35 55

^a All reactions were carried out in CCl₄ (ca 5 equiv.) under Ar atmosphere using PdCl₂ as a catalyst.

Heating above 80° for 7–12 hr is required to attain high yields. Secondary alcohols are oxidised to ketones. On the other hand, aliphatic primary alcohols are converted to esters. Typically, 1-octanol was converted to octyl octanoate. Oxidation of primary alcohols to esters is known with other oxidants such as Na₂Cr₂O₇–H₂SO₄.¹³ The reaction is considered to involve three elemental reactions; (1) oxidation to aldehyde, (2) formation of a hemiacetal from aldehyde and alcohol and (3) oxidation of the hemiacetal to ester. The reaction of benzyl alcohol is somewhat different, giving a mixture of benzaldehyde, benzyl benzoate, and dibenzyl ether in 70% yield in a ratio of 57:35:8.

GLC analysis of the reaction mixture revealed the formation of an equimolar amount of CHCl₃ to the ketone, and hence the reaction can be expressed by the following equation:



The role of K₂CO₃ is to neutralise HCl formed. In the absence of K₂CO₃, HCl reacts with alcohols to form the

corresponding alkyl chloride and other by-products, lowering yields of the oxidation.

2. Reaction of allylic alcohols⁸

As described in the preceding paper, polyhaloalkanes readily undergo addition reaction to olefins with Pd catalysts.¹ On the other hand, alcohols are oxidised under conditions similar to the addition reaction, as described above. In the reaction of BrCCl₃ or CCl₄ with allylic alcohols bearing a terminal olefinic bond, we have discovered a new reaction pattern, in which introduction of the trichloromethyl group at terminal carbon and oxidation of the OH group take place concomitantly (Scheme 2). For example, 1-hepten-3-ol (1) was converted to 1,1,1-trichloro-4-octanone (2) in 62% yield with BrCCl₃, and 39% yield with CCl₄. Pd(OAc)₂ combined with phosphines is a good catalyst at 100–110°. As the ligand, tris(*o*-tolyl)phosphine {P(*o*-Tol)₃}, afforded higher yields of 2 than PPh₃ as shown in Table 2. Since the reaction involves formation of HCl or HBr, the presence of base is essential. K₂CO₃ was satisfactory, but NaOAc and Bu₃N were not.

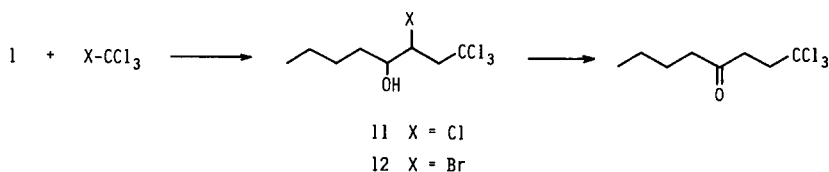
Table 2. Reaction of 1-hepten-3-ol with BrCCl₃ or CCl₄^a

$ \begin{array}{c} \text{CH}_3(\text{CH}_2)_3\text{CH}=\text{CHCH}_2\text{OH} \\ \text{1} \end{array} + \text{X-CCl}_3 \xrightarrow{[\text{Pd}]} \begin{array}{c} \text{CH}_3(\text{CH}_2)_3\text{C}(=\text{O})\text{CH}_2\text{CCl}_3 \\ \text{2} \end{array} $					
Entry	X	Ligand	Cat. (%)	Time (hr)	Yields ^b (%)
1	Br	PPh ₃	5	3	26
2	Br	P(<i>o</i> -Tol) ₃	5	3	85 (62) ^c
3	Br	P(<i>o</i> -Tol) ₃	1	3	52
4	Br	P(<i>o</i> -Tol) ₃	0.2	3	9
5	Cl	P(<i>o</i> -Tol) ₃	5	18	39 ^c

^a All reactions were carried out with Pd(OAc)₂/PR₃ (1:2) in the presence of K₂CO₃ (200 mol%) in benzene at 110° under argon atmosphere.

^b Determined by GLC.

^c Isolated yields.



Scheme 3.

We observed an interesting temperature effect on the reaction course. The reaction of **1** with BrCCl_3 or CCl_4 below 40° afforded 3-bromo-1,1,1-trichloro-4-octanol (**11**) and 1,1,1,3-tetrachloro-octane (**12**), as the simple adducts, selectively. Monitoring the reaction at 60 – 80° by TLC, we observed the increase of the trichloro ketone **2** with decrease of the simple adducts **11** or **12**. These results suggest that the adduct is the precursor of the trichloro ketone.

Other examples are shown in Table 3. In all cases, the corresponding trichloro ketones were obtained selectively at 100 – 110° in 40 – 90% yields. From the allylic alcohols possessing a Me group at the 2-position, trichloro ketones were formed even at 40° , and the adducts were hardly detected. Smooth trichloro ketone formation was not observed with allylic alcohols bearing an internal olefinic bond or primary OH group. In the former case, introduction of a trichloromethyl group is slow because of steric hindrance, and hence simple oxidation of the OH group occurred predominantly. Thus, cinnamyl alcohol was converted to a mixture of products containing cinnamaldehyde. Also the reaction of 2-propen-1-ol with BrCCl_3 afforded a complicated mixture. 2-Methyl-2-propen-1-ol (**6**) was converted to the corresponding trichloro aldehyde **10** at 40° , but the reaction at 100 – 110° gave a complicated mixture. Attempted reaction of 2-phenyl-2-propen-1-ol with BrCCl_3 afforded an intractable product.

3. Palladium-catalysed conversion of halohydrins to ketones¹¹

As described above, the simple adducts are formed at the initial stage of the reaction of polyhaloalkanes with

allylic alcohols or in the reaction carried out below 40° . We have found that treatment of these adducts with a catalytic amount of $\text{Pd}(\text{OAc})_2$ combined with $\text{P}(o\text{-Tol})_3$ in the presence of K_2CO_3 at 110° affords the corresponding trichloro ketones in high yields. In other words, Pd-catalysed conversion of halohydrins to ketones is possible. The results are summarised in Table 4. In the absence of Pd, only a trace of the ketones was obtained. By the use of other phosphines such as PPh_3 , tricyclohexylphosphine and 1,2-bis(diphenylphosphino)ethane, the ketones were obtained in lower yields. Benzene or toluene is a suitable solvent, and use of polar solvents such as alcohols, MeCN and THF gives considerable amounts of epoxides, which are considered to be formed by the reaction of halohydrins with K_2CO_3 .

This Pd-catalysed conversion of halohydrins to ketones can be applied to other halohydrins. Halohydrins bearing secondary or tertiary halides are converted to the corresponding ketones in high yields. In the cases of halohydrins bearing terminal halides concomitant formation of epoxides is a serious side reaction and the ketones are obtained in moderate yields. Pd-catalysed conversion of epoxides to ketones did not occur.

A similar conversion of halohydrins to ketones with Grignard reagent or silver salts was reported by House.¹⁴ Very recently, a Co-catalysed reaction was reported.¹⁵ The Pd-catalysed reaction is a very convenient method to give ketones in satisfactory yields. As one example, we carried out regioselective oxidation of iso-safrole to 1-(3,4-methylenedioxyphenyl)-1-propanone (**22**). Treatment of iso-safrole with N-bromosuccinimide in aqueous DMSO¹⁶ gave

Table 3. Reactions of various 1-alken-3-ols with CCl_4 and BrCCl_3 ^a

Entry	Substrates	X	Temp. (°)	Time (hr)	Cat. (%)	Products	Yields (%)
1		Br	110	4	1		43
2		Br Br	40 110	13 5	1 1		80 51
3		Br Br Cl	40 110 110	8 4 7	1 1 1		55 87 50
4		Br	40	5	1		58

^a All reactions were carried out in the presence of $\text{Pd}(\text{OAc})_2$ (1 mol%), $\text{P}(o\text{-Tol})_3$ (2 mol%), and K_2CO_3 (200 mol%) under argon atmosphere.

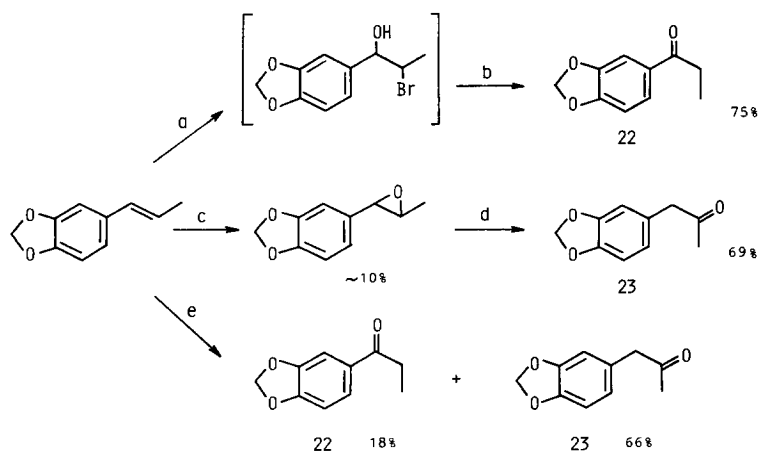
Table 4. Conversion of halohydrins to ketones

Entry	Adducts	Products	Yields (%) ^a
1			87
2			57
3			87
4			87
5			63
6			68
7			79
8			28 (34) 44 (22) 46 (20)
9			41 (28)

^a Yields of the epoxides are shown in parentheses.

bromohydrin in a quantitative yield. Successive treatment of the bromohydrin with $\text{Pd}(\text{OAc})_2$ (5 mol %) combined with $\text{P}(o\text{-Tol})_3$ (10 mol %) in the presence of K_2CO_3 , gave **22** in 75% yield. No regio-isomeric ketone was obtained. Epoxidation of iso-safrole with *m*-CPBA

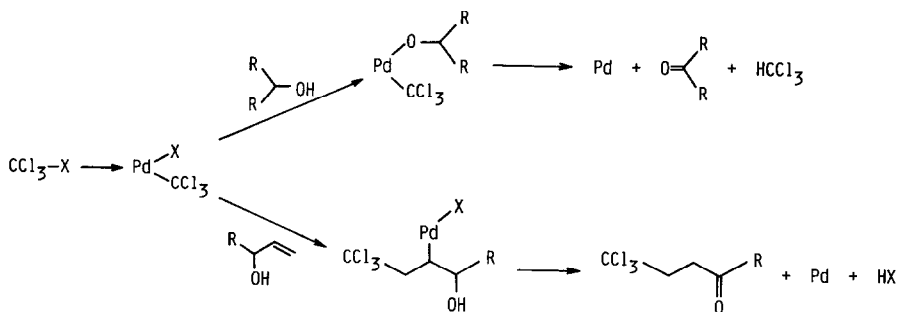
followed by treatment with $\text{BF}_3\cdot\text{OEt}_2$ afforded **23** as the sole product. Furthermore, direct oxidation of iso-safrole with $\text{PdCl}_2/\text{CuCl}$ catalyst under oxygen atmosphere afforded **22** and **23** in 18 and 66% yields, respectively. These results imply that the preparative



a. NBS / DMSO aq. .

b. $\text{Pd}(\text{OAc})_2 / \text{P}(o\text{-Tol})_3 / \text{K}_2\text{CO}_3$.c. *m*-CPBA.d. $\text{BF}_3\cdot\text{OEt}_2 / \text{Et}_2\text{O}$.e. $\text{PdCl}_2 / \text{CuCl} / \text{O}_2$.

Scheme 4.



Scheme 5.

method of ketones from olefins via bromohydrins is useful, especially when the bromohydrins are formed from olefins with high selectivity.

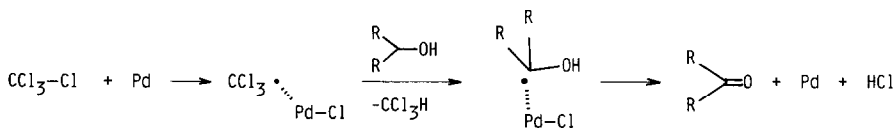
4. Mechanistic consideration

The oxidation of alcohols with CCl_4 , and formation of trichloroketones reported in this paper correspond to the oxidation of alcohols with aryl halides,⁵⁻⁷ and formation of β -aryl ketones from allylic alcohols and aryl halides.^{9,10} Thus, one may expect that the reactions proceed via a mechanism similar to the reactions of aryl halides, namely oxidative addition of polyhaloalkanes to $\text{Pd}(0)$, followed by nucleophilic substitution of halide on Pd by alkoxide and successive β -hydride elimination, or followed by insertion of olefinic bond of allylic alcohols and successive β -hydride elimination (Scheme 5). However, results described below do not necessarily support this mechanism.

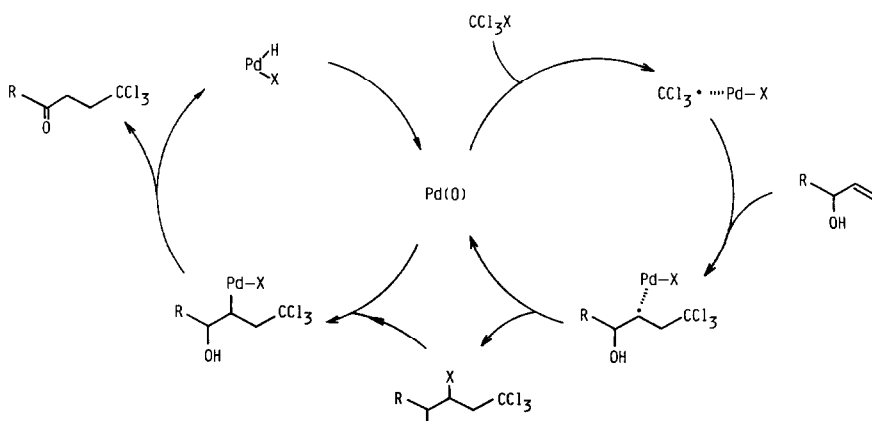
It is known that CCl_4 or 1,1,1-trichloroalkanes are reduced in alcoholic media to CHCl_3 or 1,1-dichloroalkanes, respectively, by the catalysis of $\text{RuCl}_2(\text{PPh}_3)_3$.¹⁷ Alcohols act as hydrogen donors and a trapper of HCl is formed. Thus, from isopropanol, a mixture of acetone and 2-chloropropane is formed. In the Ru-catalysed reaction, we found that presence of K_2CO_3 leads to successful oxidation of alcohols with

CCl_4 at an elevated temperature without forming the corresponding chloride. Similarly, other transition metal catalysts active for the addition of CCl_4 to olefins are also active, more or less, for the oxidation of alcohols under similar conditions. These reactions can be explained by H-abstraction from alcohol by the trichloromethyl radical generated by transition metal catalysts. As described in the preceding papers, the trichloromethyl radical is considered to be formed by the action of $\text{Pd}(0)$, and hence, a mechanism illustrated in Scheme 6 is proposed.

In contrast, the formation of trichloro ketones cannot be accomplished by other transition metal catalysts or under free radical conditions. Asscher and Vofsi reported simple addition of CCl_4 to 2-propen-1-ol with Fe catalysts,¹⁸ and similar simple addition of CCl_4 or BrCCl_3 to 1-hepten-3-ol was confirmed by us by the catalysis of $\text{RuCl}_2(\text{PPh}_3)_3$ or $(\text{PhCO}_2)_2$. However, the Pd-catalysed formation of trichloro ketones seems to involve the simple addition, followed by the conversion of halohydrins formed to ketones. In both steps, catalysis by Pd is essential. The mechanism of the Pd-catalysed conversion of halohydrins to ketones is not clear, but may involve oxidative addition of the carbon-halogen bond onto $\text{Pd}(0)$ and successive β -hydride elimination. The overall process is illustrated in Scheme 7.



Scheme 6.



Scheme 7.

EXPERIMENTAL

General

NMR spectra were taken on a Hitachi R-24A (60 MHz) or R-40 (90 MHz) spectrometer. The chemical shifts are recorded by δ units in ppm relative to TMS. IR spectra were taken with a JASCO IRA-2 spectrometer and recorded in wave number. The known products were identified by comparison of spectral data with those of authentic samples. Physical data of new compounds are shown below.

General procedure for the oxidation of alcohols with CCl_4

To a mixture of PdCl_2 (2 mg, 0.01 mmol) and K_2CO_3 (138 mg, 1 mmol) was added alcohol (1 mmol) dissolved in excess CCl_4 . The suspension was refluxed under argon. After the reaction was complete, K-salt was filtered off, and the filtrate was concentrated. Purification of the residue by column chromatography (silica gel, hexane-ether) afforded the desired ketone or ester. In some cases, the reaction was carried out in a pressure bottle at 110° .

General procedure for the 4,4,4-trichloro ketone formation from allylic alcohols and BrCCl_3 or CCl_4

In a pyrex tube fitted with a screw cap, were placed $\text{Pd}(\text{OAc})_2$ (2 mg, 0.01 mmol), $\text{P}(o\text{-Tol})_3$ (6 mg, 0.02 mmol) and K_2CO_3 (276 mg, 2 mmol). A benzene soln of allylic alcohol (1 mmol) and BrCCl_3 (198.3 mg, 1 mmol) was added, and the mixture was heated at 110° for several hr. After removal of the solvent, the mixture was purified by column chromatography (silica gel, hexane-ether) to give the corresponding ketone. Application of 5 equiv. of CCl_4 also afforded the desired ketone.

1,1,1-Trichloro-4-octanone (2). NMR (90 MHz, CDCl_3) 0.7–1.1 (m, 3H, CH_3), 1.1–1.9 (m, 4H, alkyl), 2.33–2.70 (m, 2H, CH_2CO), 2.70–3.20 (m, 4H, $\text{COCH}_2\text{CH}_2\text{CCl}_3$); IR (neat) 1720, 780, 690; m/e 230 (M), 232 (M+2), 234 (M+4); high resolution mass: calc for $\text{C}_8\text{H}_{13}\text{OCl}_3$ (M): 230.0026; found: 230.0001.

1-Phenyl-4,4,4-trichloro-1-butanone (7). NMR (90 MHz, CDCl_3) 3.0–3.7 (m, 4H, $\text{COCH}_2\text{CH}_2\text{CCl}_3$), 7.3–8.25 (m, 5H, phenyl); IR (neat) 1690, 1600, 1580, 750, 690; m/e 250 (M), 252 (M+2), (M+4); high resolution mass: calc for $\text{C}_{10}\text{H}_9\text{OCl}_3$: 249.9718; found: 249.9723.

3-Methyl-1,1,1-trichloro-4-octanone (8). NMR (90 MHz, CDCl_3) 0.8–1.1 (m, 3H, CH_3), 1.1–1.8 (m, 4H, alkyl), 1.23 (d, 3H, $J = 7.5$ Hz, CH_3CHCO), 2.4–2.76 (m, 3H, $\text{CCl}_3\text{CH}_2\text{COCH}_2$), 3.1 (m, 1H, CHCO), 3.6 (dd, 1H, $J = 7.5, 15$ Hz, CCl_3CH); IR (neat) 1720, 770, 700; m/e 244 (M), 246 (M+2), 248 (M+4); high resolution mass: calc for $\text{C}_9\text{H}_{15}\text{OCl}_3$: 244.0187; found: 244.0156.

2-Methyl-1-phenyl-4,4,4-trichloro-1-butanone (9). NMR (90 MHz, CDCl_3) 1.31 (d, 3H, $J = 7.5$ Hz, CH_3), 2.75 (d, 1H, broad, CCl_3CH), 3.63–4.20 (m, 2H, $\text{CCl}_3\text{CHCHCO}$), 7.35–8.25 (m, 5H, phenyl); IR (neat) 1680, 1600, 1580, 780, 743, 705; m/e 264 (M), 266 (M+2), 268 (M+4); high resolution mass: calc for $\text{C}_{11}\text{H}_{11}\text{OCl}_3$: 263.9872; found: 263.9847.

2-Methyl-4,4,4-trichlorobutanal (10). NMR (90 MHz, CDCl_3) 1.33 (d, 3H, $J = 7.5$ Hz, CH_3), 2.60 (dd, 1H, $J = 4, 15$ Hz, CHCCl_3), 2.82–3.16 (m, 1H, CHCH_3), 3.53 (dd, 1H, $J = 6, 15$ Hz, CHCCl_3), 9.8 (s, 1H, CHO); IR (neat) 1735, 910, 775, 700. (Calc for $\text{C}_5\text{H}_7\text{OCl}_3$: C, 31.70; H, 3.72; Cl, 56.14. Found: C, 31.60; H, 3.69; Cl, 57.89%.) B.p. $78^\circ/12$ mmHg.

Preparation of allylic alcohols. Allylic alcohols **1** and **3–5** were prepared from acrolein or methacrolein with $n\text{-BuLi}$ or PhMgBr .

2-Methyl-1-phenyl-2-propen-1-ol (5). NMR (60 MHz, CCl_4) 1.55 (s, 3H, allylic), 2.6 (s, 1H, OH), 4.7–5.3 (m, 3H, CHOH , olefinic), 7.3 (s, 5H, phenyl); IR (neat) 3400, 1650, 905. (Calc for $\text{C}_{10}\text{H}_{12}\text{O}$: C, 81.04; H, 8.16. Found: C, 80.67; H, 8.45%.)

Preparation of halohydrins. The halohydrins **11–13** were prepared following the procedure described in the preceding paper,⁸ and **14–16** were prepared by reaction of olefins with N -bromosuccinimide in aqueous DMSO.¹⁶ The compounds **17–21** were prepared by the reduction of the corresponding halo ketones with NaBH_4 in ethanol.

3-Bromo-1,1,1-trichloro-4-octanol (11). NMR (60 MHz, CCl_4) 0.7–1.15 (m, 3H, CH_3), 1.15–1.9 (m, 6H, alkyl), 1.9–2.2 (m, 1H, OH), 3.2–3.35 (m, 2H, CCl_3CH_2), 3.35–3.75 (m, 1H, CHOH), 4.15–4.45 (m, 1H, CHBr); IR (neat) 3400, 2950, 800, 705. (Calc for $\text{C}_8\text{H}_{14}\text{OBrCl}_3$: C, 30.75; H, 4.52; Br + Cl, 59.61. Found: C, 30.53; H, 4.63; Br + Cl, 59.95%.)

1,1,1,3-Tetrachloro-4-octanol (12). NMR (60 MHz, CCl_4) 0.7–1.1 (m, 3H, CH_3), 1.1–1.9 (m, 6H, alkyl), 2.0–2.4 (m, 1H, OH), 3.0–3.5 (m, 2H, CH_2CCl_3), 3.5–4.0 (m, 1H, CHOH), 4.05–4.4 (m, 1H, CHCl); IR (neat) 3400, 2920, 785, 700. (Calc for $\text{C}_8\text{H}_{14}\text{OCl}_4$: C, 35.85; H, 5.27; Cl, 52.91. Found: C, 35.62; H, 5.16; Cl, 53.33%.)

2-Bromo-1-phenyl-4,4,4-trichloro-1-butanol (13). NMR (60 MHz, CCl_4) 2.7–2.8 (m, 1H, OH), 3.05–3.25 (m, 2H, CCl_3CH_2), 4.12–4.50 (m, 1H, BrCH), 4.8–5.1 (m, 1H, CHOH), 7.2 (s, 5H, phenyl); IR (neat) 3300, 2900, 790, 700. (Calc for $\text{C}_{10}\text{H}_{10}\text{OBrCl}_3$: C, 36.13; H, 3.03. Found: C, 36.30; H, 2.94%.)

General procedure for the conversion of halohydrins to ketones

In a flask fitted with a reflux condenser were placed $\text{Pd}(\text{OAc})_2$ (2 mg, 0.01 mmol), $\text{P}(o\text{-Tol})_3$ (6 mg, 0.02 mmol), and K_2CO_3 (138 mg, 1 mmol), and the atmosphere was replaced by argon. Halohydrin (1 mmol) dissolved in benzene (2 ml) was added, and the suspension was refluxed for several hr under argon. The K-salts were filtered off, and the filtrate was purified by column chromatography (silica gel, ether-hexane) to give the ketone.

Oxidation of iso-safrole

Method A (via bromohydrin). Bromohydrin was prepared from iso-safrol according to the procedure of Dalton *et al.*¹⁶ In a pyrex tube fitted with a screw cap were placed $\text{Pd}(\text{OAc})_2$ (11.2 mg, 0.05 mmol), $\text{P}(o\text{-Tol})_3$ (30.4 mg, 0.1 mmol) and K_2CO_3 (138 mg, 1 mmol) under argon. The bromohydrin (259 mg, 1 mmol) dissolved in benzene (1 ml) was added, and then the mixture was heated at 100° for 5 hr. After the work-up as above, purification of the residue by column chromatography (silica gel, hexane-ether) afforded the desired **22**.

Method B (via epoxide). To a soln of iso-safrole (1.62 g, 10 mmol) in CH_2Cl_2 (10 ml) was added $m\text{CPBA}$ (3.24 g, 15 mmol) dissolved in CH_2Cl_2 (10 ml). The mixture was stirred at 0° for 30 min. Usual work-up and chromatographic purification (silica gel, hexane-ether) afforded the epoxide (190 mg) in 11% yield. The epoxide (190 mg, 1.07 mmol) was treated with $\text{BF}_3\text{-OEt}_2$ (1 ml) in ether at room temp for 20 min. The soln was quenched with NaHCO_3 aq, and the ethereal layer was washed with brine and dried over MgSO_4 . After removal of the solvent, the residue was purified by column chromatography (silica gel, hexane-ether) to give **23** in 69% yield (132 mg).

Method C (the Wacker oxidation). In a flask fitted with a balloon filled with O_2 were placed PdCl_2 (35.5 mg, 0.2 mmol) and CuCl (79.2 mg, 0.8 mmol) in aqueous DMF (DMF- H_2O 7:1, 2 ml). The suspension was stirred under O_2 at room temp for 2 hr. Then, iso-safrole (324.4 mg, 2 mmol) dissolved in the aqueous DMF (2 ml) was introduced, and the mixture was heated at 50° for 10 hr. Usual work-up and purification by column chromatography (silica gel, hexane-ether) afforded **22** (236 mg, 66%) and **23** (65 mg, 18%).

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