Transition Metal Catalyzed Intramolecular Cyclizations of (Trichloromethyl)alkenes

Gary M. Lee and Steven M. Weinreb*

Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802

Received July 18, 1989

Intramolecular Kharasch cyclizations of a variety of functionalized olefinic trichloromethyl substrates are promoted by transition-metal complexes. The regioselectivity of the cyclization is critically dependent upon the structure of the trichloromethyl compound. Thus, trichloromethyl substrate **1** afforded primarily five-membered ring exo closure product **8**, as did **5a** and **6**, yielding mainly trichloro alcohol **12**. Similarly trichloroalkene **2** gave primarily the six-membered ring exo closure product **10**. Trichloromethyl ketones **7a–c**, on the other hand, produced predominantly endo closure products.

Introduction

Previous recent publications from these laboratories have described construction of highly functionalized carbocyclic systems via transition metal mediated intramolecular Kharasch radical cyclizations.[1] To date we have reported efficient cyclizations of olefinic α,α-dichloro esters, acids, and nitriles,[1a,b] as well as mono-α-chloro and -α-bromo esters and acids,[1c] catalyzed by iron, ruthenium, copper, and molybdenum complexes. In order to further explore the scope and limitations of this methodology, we have prepared a number of other structurally diverse chloroalkenes and subjected these substrates to the cyclization conditions using various metal catalysts. These studies are described in this paper.

Synthesis of Cyclization Substrates

The chloroalkenes used in this work were readily prepared by one of the two routes shown in eq 1 and in Scheme I. Alkylation of the carbanion derived from butyllithium deprotonation of chloroform with iodoalkenes gave the trichloromethyl compounds **1-3** (eq 1). Interestingly, this carbanion has apparently not previously been alkylated with alkyl halides, although its addition to carbonyl compounds is known.[2] However, the related carbanions derived from methylene chloride and 1,1-dichloroalkanes have been combined with simple alkyl bromides and iodides.[3]

$$CHCl_3 \xrightarrow[\text{2) } RCH_2I/HMPA]{\text{1) BuLi/THF, -100 °C}} RCH_2CCl_3 \qquad \text{(Eq 1)}$$

1 R = $CH_2CH_2CH{=}CH_2$

2 R = $CH_2CH_2CH_2CH{=}CH_2$

3 R = 

Addition of lithio trichloromethane to aldehydes **4a–c** afforded trichloromethyl alcohols **5a–c**, respectively (Scheme I).[2] Alcohol **5a** was converted to the *tert*-butyldimethylsilyl ether **6** by the standard procedure. In addition, alcohols **5a–c** were converted to the trichloromethyl ketones **7a–c** by chromate oxidation.

Cyclization Studies

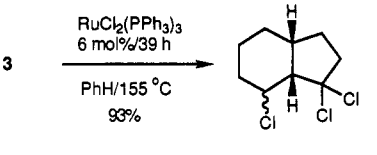
We initially investigated the cyclization of trichloromethyl olefin **1** using a number of different transition-metal catalysts.[4] Reactions were conducted in a sealed tube in degassed benzene at 155 °C using the metal complexes shown in Table I. As can be seen, the ferrous chloride/triethyl phosphite[5] and ruthenium catalysts afforded the best yields of cyclization products.[6] As was anticipated, the preferred mode of cyclization occurred via exo closure of a putative metal-coordinated 5-hexenyl radical giving **8**.[1,7] Small amounts of the endo closure product **9** were also produced.

The homologous trichloromethyl substrate **2** was subjected to similar cyclization conditions (Table I). Once again, the ruthenium and iron catalysts proved most effective, and the exo closure product **10** predominated. However, significant amounts of the seven-membered ring compound **11** were also found.[6]

Cyclization studies have also been conducted with the more highly functionalized substrates prepared in the scheme. For example, trichloromethyl alcohol **5a** could be cyclized with both the iron and ruthenium catalysts to **12** and **13** (Table I). The exo closure product **12** proved to be a mixture of diastereomers in the yields shown,[6] but stereochemistry of the individual products was not established. The six-membered ring endo product **13**, formed in only small amount, is a single isomer.

Silyl ether **6** also underwent cyclization with the ruthenium catalyst, but surprisingly not with the iron complex (Table I). In this case, a slightly better degree of stereoselectivity was found for the exocyclic closure.

In order to acertain whether this cyclization procedure could be used in a short annulation sequence, trichloromethyl compound **3** was treated with the ruthenium catalyst (eq 2). We were pleased to find that **3** cyclized cleanly to a single [6,5]-fused system **14**.



(Eq 2)

14

In light of a report that methylene chloride could be added to olefins intermolecularly in modest yields using

(1) (a) Hayes, T. K.; Freyer, A. J.; Parvez, M.; Weinreb, S. M. *J. Org. Chem.* **1986**, *51*, 5501. (b) Hayes, T. K.; Villani, R.; Weinreb, S. M. *J. Am. Chem. Soc.* **1988**, *110*, 5533. (c) Lee, G. M.; Parvez, M.; Weinreb, S. M. *Tetrahedron* **1988**, *44*, 4671.

(2) Taguchi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 3010. Kobrich, G.; Flory, K.; Dischel, W. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 513. See also: Kobrich, G.; Flory, K.; Merkle, H. R. *Tetrahedron Lett.* **1965**, 972. Castro, B.; Villieras, J. *C. R. Acad. Sci, Paris Ser. C* **1967**, *264*, 1609.

(3) Villieras, J.; Perriot, P.; Normant, J. F. *Bull. Soc. Chim. Fr.* **1977**, 765. Villieras, J.; Perriot, P.; Normant, J. F. *Synthesis* **1979**, 502.

(4) For references to intermolecular metal catalyzed additions of $HCCl_3$ to alkenes, see: Minisci, F. *Acc. Chem. Res.* **1975**, *8*, 165. See also: Watanabe, Y.; Endo, T. *Tetrahedron Lett.* **1988**, *29*, 321.

(5) Ittel, S. D.; English, A. D.; Tolman, C. A.; Jessen, J. P. *Inorg. Chim. Acta* **1979**, *33*, 101.

(6) Yields were determined by GLC analysis. Compounds were isolated and characterized in pure form unless otherwise noted.

(7) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073.

0022-3263/90/1955-1281$02.50/0

Scheme I

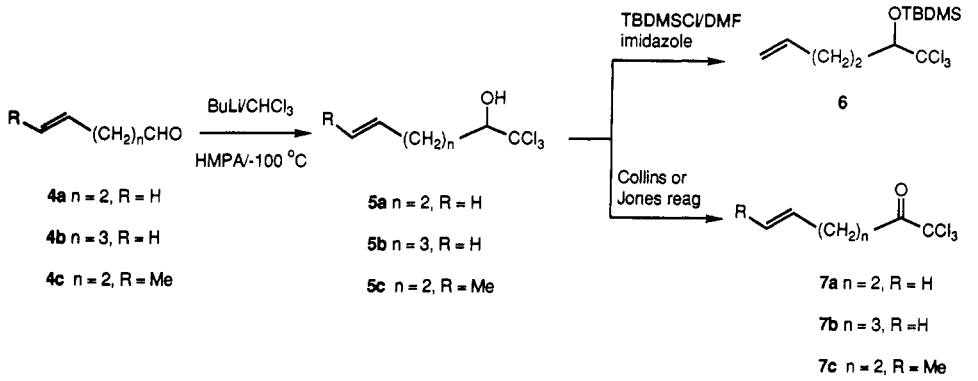
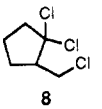
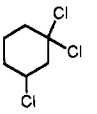
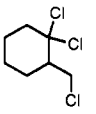
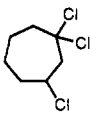
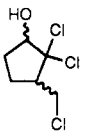
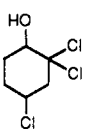
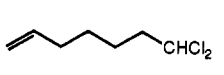


Table I. Cyclizations of (Trichloromethyl)alkenes[a]

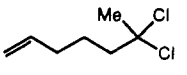
substrate	catalyst	mol %	time, h	products (% yield[6])	recovered starting material, %
				 + 	
				8 + 9	
1	$RuCl_2(PPh_3)_3$	5	41	79 + 9	7
	$FeCl_2[P(OEt)_3]_3$	11	41	79 + 10	–
	$[CpMo(CO)_3]_2$	9	40	11 + 1	32
	$Fe(CO)_5$	8	42	2 + 1	65
				 + 	
				10 + 11	
2	$RuCl_2(PPh_3)_3$	6	44	68 + 16	
	$FeCl_2[P(OEt)_3]_3$	10	70	75 + 13	
	$[CpMo(CO)_3]_2$	5	42	21 + –	
				 + 	
				12 + 13	
5a	$RuCl_2(PPh_3)_3$	2	89	41/27 + 5	
	$FeCl_2[P(OEt)_3]_3$	10	42	30/24 + 5	
6[b]	$RuCl_2(PPh_3)_3$	11	43	44/6 + 5	

[a] Reactions run in benzene at 155 °C. [b] Crude product treated with Et_4NF before analysis.

$NiCl_2(PPh)_2$ as catalyst,[8] we attempted cyclizations of isomeric dichloroheptenes **15**[9a] and **16**.[9b,10] With the nickel catalyst, neither substrate showed any inclination to cyclize. Moreover, the other catalysts listed in the table were also totally ineffective in promoting cyclization of **15** and **16**. In all cases, only starting material was recovered using reaction temperatures in the 155–160 °C range.



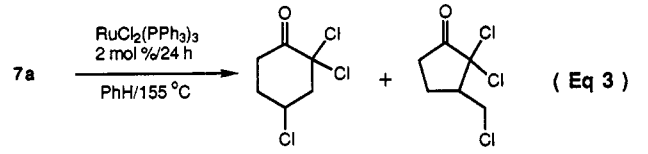
15



16

We next turned to cyclization of the trichloromethyl ketones **7a–c** and found an interesting change in the regioselectivity of the process. Treatment of **7a** with the ruthenium catalyst under the usual thermal conditions afforded predominantly the endo cyclization product **17** and only a small amount of exo closure compound **18** (eq 3). This type of reversed regioselectivity has previously been observed with some α-keto radicals.[1b,11–13] It is

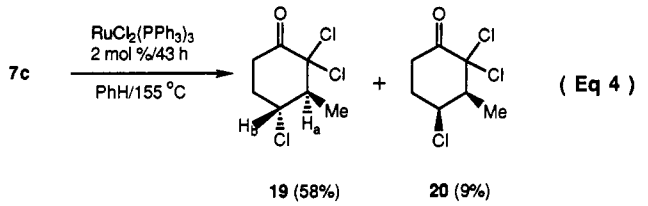
(8) Inoue, Y.; Ohno, S.; Hashimoto, H. *Chem. Lett.* **1978**, 367.
(9) (a) Prepared by alkylation of lithiodichloromethane with 6-bromo-1-hexene.[3] (b) Prepared by alkylation of lithio-1,1-dichloroethane with 5-bromo-1-pentene.[3]
(10) Lee, G. M. Ph.D. Thesis, The Pennsylvania State University, 1990.
(11) (a) Clive, D. L. J.; Cheshire, D. R. *J. Chem. Soc., Chem. Commun.* **1987**, 1520. (b) Clive, D. L. J. *Pure Appl. Chem.* **1988**, *60*, 1645.
(12) Curran, D. P.; Chang, C.-T. *J. Org. Chem.* **1989**, *54*, 3140.



(Eq 3)

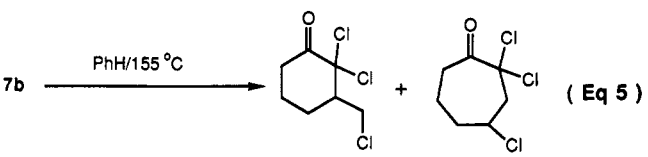
possible that this selectivity is the result of a kinetic ring closure governed by stereoelectronic effects.[11] Alternatively, this result could be due to a reversible cyclization, as is often the case with highly stabilized radicals.[13]

Another system which we briefly investigated was substituted alkene **7c** (eq 4). Ruthenium-promoted cyclization of this compound afforded only endo closure products **19** and **20**.[6] The major cyclization product **19** was assigned the trans stereochemistry shown based upon ^{1}H NMR coupling constants (J_{ab} = ~10 Hz).



(Eq 4)

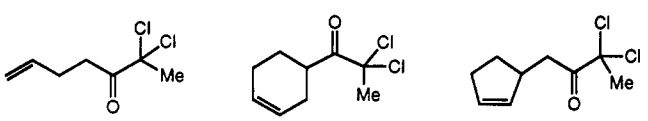
Trichloromethyl ketone **7b** was also subjected to the Kharasch cyclization (eq 5). Interestingly, **7b** afforded about 1:1 mixtures of the cyclohexanone exo closure product **21** and the cycloheptanone endo product **22** with both the iron and ruthenium catalysts. This regiochemical result is strikingly similar to that found by Clive for cyclization of a simpler nonchlorinated α-keto heptenyl radical.[11b]



(Eq 5)

$FeCl_2[(EtO)_3P]_3$ (5,5 mol %) 48 h	29%	26%
$RuCl_2(PPh_3)_3$ (2 mol %) 48 h	44%	45%

In an attempt to further extend the methodology, α,α-dichloro ketones **23**, **24**, and **25** were examined as cyclization substrates.[14] Treatment of these compounds with a variety of iron, ruthenium, copper, molybdenum, and nickel catalysts gave only small amounts of mono reductive dechlorination products along with recovered starting material.



23 24 25

Conclusion

We have demonstrated that a variety of olefinic trichloromethyl compounds are reliable substrates in intramolecular metal promoted Kharasch cyclizations. In the cases of simple trichloromethyl olefins like **1–3** and the α-oxy systems (cf. **5**, **6**) cyclization occurs via the normal exo mode expected for 5-hexenyl radicals.[7] With α-keto radicals derived from trichloromethyl ketones a reversal of regiochemistry was observed. It appears that there is a general tendency for α-keto radicals in which the carbonyl group is endocyclic to the ring being formed to close via an endo mode. Thus, α-keto 5-hexenyl radicals give cyclohexanones rather than cyclopentanones, and there is even a tendency for the heptenyl analogues to yield cycloheptanones.[1,11–13]

The failure of dichloroalkenes **15** and **16** to cyclize is not too surprising considering the fact that methylene chloride is not particularly effective in intermolecular Kharasch additions to alkenes.[8] More puzzling, however, is the fact that dichloro ketones **23**, **24**, and **25** do not cyclize since we have previously found that α,α-dichloro esters and nitriles, and even mono-α-chloro esters cyclize efficiently.[1] It is not clear if the problem with **23–25** is in initial formation of the metal complexed radical[16] or in the cyclization step itself. We are continuing to explore and extend this methodology.

Experimental Section

Proton nuclear magnetic resonance spectra (^{1}H NMR) were obtained at 300 MHz on a Bruker AM 300 NMR spectrometer, at 200 MHz on a Bruker WP-200 instrument, and at 360 MHz on a Bruker WP-360 spectrometer. Carbon-13 magnetic resonance spectra (^{13}C NMR) were recorded at 75 MHz on a Bruker AM 300 spectrometer. Low- and high-resolution mass spectra (MS) were obtained at 50–70 eV by electron impact on a Kratos MS9/50 double-focusing mass spectrometer. Combustion analyses were performed by Midwest Microlab (Indianapolis, IN). Both analytical and preparative thin-layer chromatography (TLC) were performed using E. M. Merck silica gel PF-254. Flash and "dry column" flash chromatography were done using Baker silica gel (25–40 mm) according to the procedures of Still[17] and Harwood,[18] respectively. Gas–liquid chromatography (GLC) was done on a Varian Model 3700 instrument equipped with a thermal conductivity detector using a 6 ft × $^1/_8$ in. stainless steel 3% SE 30 on 80/100 Supelcoport column, 10 ft × $^1/_8$ in. stainless steel 10% Carbowax 20 M on 80/100 Chromosorb WAW column, or an Alltech 10 m × 0.53 mm FSOT Superox polyethylene glycol column. High-performance liquid chromatography (HPLC) was performed using a Beckman 10 mm × 25 cm 5 μm Ultrasphere column on a Waters Model 590 pump equipped with a R401 differential refractometer and a UK6 injector.

1,1,1-Trichloro-5-hexene (1). Chloroform (0.72 mL, 9.0 mmol) was dissolved in 18 mL of dry THF and cooled to −100 °C. Butyllithium (1.40 M, 5.6 mL, 7.8 mmol) was added dropwise, and the mixture was stirred for an additional 10 min at which time a white precipitate appeared. 1-Iodo-4-pentene (1.1 g, 5.5 mmol) in 5 mL of dry THF was slowly added by syringe pump followed by HMPA (0.15 mL, 8.6 mmol) in 5 mL of dry THF. The reaction mixture was stirred for 30 min at −100 °C and then warmed slowly to −75 °C. The mixture was diluted with 1 mL of methanol, 5 mL of 5% HCl, and 30 mL of ether. The organic layer was washed with 5% HCl and brine and dried over sodium sulfate. Removal of the solvent in vacuo gave an oil, which was purified by "dry column" flash chromatography (hexane) to give 0.70 g (68%) of 1,1,1-trichloro-5-hexene (1) as a colorless oil [bp 40 °C (~30 Torr, bulb-to-bulb)]: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.9–5.7 (1 H, m), 5.1–5.0 (2 H, m), 2.69 (2 H, t, J = 8.0 Hz), 2.2–2.1 (2 H, m), 2.0–1.9 (2 H, m); IR (film) 3080, 2940, 1640, 1460, 1440, 1130, 1070, 1050, 1000, 910, 870, 780, 700 cm^{-1}; ^{13}C NMR (75 MHz,

(13) Snider, B. B.; Patricia, J. J. *J. Org. Chem.* **1989**, *54*, 38.
(14) Prepared from lithio 1,1-dichloroethane[9] and the corresponding *N*-methyl-*N*-methoxyamide.[10,15]
(15) Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815.
(16) For mechanistic studies of the metal catalyzed intermolecular addition of halocarbons to alkenes, see: Davis, R.; Groves, I. F. *J. Chem. Soc., Dalton Trans.* **1982**, 2281. Bland, W. J.; Davis, R.; Durrant, J. L. A. *J. Organomet. Chem.* **1984**, *260*, C75. Bland, W. J.; Davis, R.; Durrant, J. L. A. *J. Organomet. Chem.* **1984**, *267*, C45.
(17) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(18) Harwood, L. M. *Aldrichchimica Acta* **1985**, *18*, 25.

$CDCl_3$) δ 137.1, 115.8, 100.0, 54.5, 32.2, 25.5; MS *m/z* (relative intensity) 188 (0.7), 186 (0.7), 153 (8), 151 (12), 117 (40), 115 (86).

1,1,1-Trichloro-6-heptene (2). Via the alkylation procedure for preparation of 1,1,1-trichloro-5-hexene (1), chloroform (2.4 mL, 30 mmol) was alkylated with 1-iodo-5-hexene (5.0 g, 24 mmol) to give, after purification by flash chromatography (hexane), 4.3 g (90%) of 1,1,1-trichloro-6-heptene (2) as a yellow oil: ^1H NMR (200 MHz, $CDCl_3$) δ 5.9–5.7 (1 H, m), 5.1–5.0 (2 H, m), 2.69 (2 H, t, *J* = 7.9 Hz), 2.2–1.5 (6 H, m); IR (film) 3080, 2920, 2860, 1640, 1450, 1130, 1070, 1050, 1000, 915, 790, 700 cm^{-1}; ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 115.1, 100.0, 55.0, 33.3, 27.5, 25.8; MS *m/z* (relative intensity) 202 (2.4), 200 (3.0), 93 (46), 84 (47), 68 (74), 55 (100), 49 (68), 42 (51), 41 (100), 27 (44). Anal. Calcd for $C_7H_{11}Cl_3$: C, 41.72; H, 5.50. Found: C, 41.32; H, 5.06.

3-(2-Cyclohexenyl)-1,1,1-trichloropropane (3). Via the alkylation procedure for synthesis of 1,1,1-trichloro-5-hexane (1), chloroform (0.18 mL, 2.2 mmol) was alkylated with 2-(2-cyclohexyl)-1-iodoethane (0.32 g, 1.4 mmol) to give, after purification by flash chromatography (hexane), 0.21 g (68%) of 3-(2-cyclohexenyl)-1,1,1-trichloropropane (3) as a yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 5.8–5.7 (1 H, m), 5.6–5.5 (1 H, m), 2.73 (2 H, t, *J* = 8.0 Hz), 2.2–2.1 (1 H, m), 2.0–1.8 (2 H, m), 1.8–1.7 (4 H, m), 1.6–1.5 (1 H, m), 1.4–1.3 (1 H, m); IR (film) 3060, 2950, 2870, 1620, 1450, 1300, 1270, 1215, 1100, 1050, 1020, 900, 830, 810, 700 cm^{-1}.

1,1,1-Trichloro-5-hexen-2-ol (5a). Chloroform (1.8 mL, 22 mmol) was dissolved in 40 mL of dry THF and cooled to −110 °C. Butyllithium (2.5 M, 8.0 mL, 20 mmol) was added dropwise, and the mixture was stirred for an additional 10 min. A solution of HMPA (3.5 mL, 20 mmol) in 5 mL of dry THF was added to the mixture using a syringe pump. Addition of 4-pentenal (**4a**, 1.53 g, 18.2 mmol) in 5 mL of dry THF produced a dark reaction mixture which was kept at −110 °C for 20 min and then warmed to −60 °C slowly. The reaction mixture was diluted with 1 mL of methanol, 10 mL of 5% HCl, and 30 mL of ether. The organic layer was washed with 5% HCl and brine and dried over sodium sulfate. Removal of the solvent in vacuo gave an oil, which was purified by flash chromatography (9:1, 7.5:2.5, hexane–ethyl acetate) and distillation [bp 60 °C (~30 Torr, bulb-to-bulb)] to give 2.0 g (54%) of 1,1,1-trichloro-5-hexen-2-ol (**5a**) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 5.9–5.7 (1 H, m), 5.2–5.0 (2 H, m), 4.04 (1 H, ddd, *J* = 1.8, 5.6, 9.9 Hz), 3.0–2.9 (1 H, m), 2.4–2.1 (3 H, m), 1.9–1.7 (1 H, m); IR (film) 3420, 3080, 2970, 2940, 1640, 1440, 1385, 1130, 1090, 995, 920, 830, 795 cm^{-1}; ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.1, 115.9, 104.1, 82.0, 30.5, 29.9; CIMS *m/z* 205, 203 ($M^+ + 1$).

1,1,1-Trichloro-6-hepten-2-ol (5b). Utilizing the procedure for the synthesis of 1,1,1-trichloro-5-hexen-2-ol (**5a**), 1,1,1-trichloro-6-hepten-2-ol (**5b**) was prepared. 5-Hexenal (**4b**, 1.8 g, 18 mmol) was alkylated with chloroform (1.8 mL, 22 mmol) to give after purification by distillation [bp 120 °C (~30 Torr)] 2.5 g (63%) of 1,1,1-trichloro-6-hepten-2-ol (**5b**) as a colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 5.9–5.7 (1 H, m), 5.1–5.0 (2 H, m), 4.02 (1 H, d, *J* = 8.2 Hz), 2.78 (1 H, s), 2.2–2.0 (3 H, m), 1.9–1.5 (3 H, m); IR (film) 3440, 3090, 2970, 2940, 2870, 1640, 1445, 1090, 1000, 920, 845, 820, 790 cm^{-1}; ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 115.1, 104.2, 82.8, 33.2, 30.9, 25.3.

***trans*-1,1,1-Trichloro-5-hepten-2-ol (5c).** Prepared as described for the synthesis of 1,1,1-trichloro-5-hepten-2-ol (**5a**). *trans*-4-Hexenal (**4c**, 1.9 g, 19 mmol) was alkylated with chloroform (2.1 mL, 26 mmol) to give after purification by distillation [bp 60 °C (~30 Torr, bulb-to-bulb)] 1.4 g (33%) of *trans*-1,1,1-trichloro-5-hepten-2-ol (**5c**) as a colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 5.5 (2 H, m), 4.02 (1 H, ddd, *J* = 1.6, 5.6, 9.9 Hz), 2.86 (1 H, d, *J* = 5.5 Hz), 2.3–2.0 (3 H, m), 1.8–1.7 (1 H, m), 1.67 (3 H, d, *J* = 4.8 Hz); IR (film) 3450, 3030, 2980, 2940, 2860, 1455, 1100, 980, 625 cm^{-1}.

2-(*tert*-Butyldimethylsiloxy)-1,1,1-trichloro-5-hexene (6). 1,1,1-Trichloro-5-hexen-2-ol (**5a**; 0.50 g, 2.5 mmol) and *tert*-butyldimethylsilyl chloride (0.41 g, 2.7 mmol) were dissolved in 1 mL of dry DMF. Imidazole (0.33 g, 4.9 mmol) was added, and the reaction mixture was heated at 90 °C for 2 h. The reaction mixture was diluted with 30 mL of ethyl acetate, washed with 5% HCl and brine, and dried over sodium sulfate. The solvent was removed in vacuo to give an oil, which was purified by "dry column" flash chromatography (95:5, 8:2, hexane–ethyl acetate) to give 0.42 g (54%) of silyl ether **6** as a colorless oil: ^1H NMR (360 MHz, $CDCl_3$) δ 5.9–5.8 (1 H, m), 5.1–5.0 (2 H, m), 4.09 (1 H, dd, *J* = 2.2, 7.4 Hz), 2.4–2.3 (1 H, m), 2.2 (2 H, m), 1.9–1.8 (1 H, m), 0.967 (9 H, s), 0.21 (3 H, s), 0.20 (3 H, s); IR (film) 3080, 2960, 2940, 2860, 2800, 1640, 1470, 1465, 1260, 1150, 980, 920, 855, 845, 800, 780, 725 cm^{-1}.

1,1,1-Trichloro-5-hexen-2-one (7a). 1,1,1-Trichloro-5-hexen-2-ol (**5a**; 0.20 g, 1.0 mmol) was diluted with 3 mL of acetone, and Jones reagent was added until no alcohol remained as indicated by TLC. The crude reaction mixture was filtered through a plug of glass wool, and the solvent was removed in vacuo. The remaining oil was diluted with ethyl acetate, washed with aqueous $NaHSO_3$ and brine, and dried over sodium sulfate to give after "dry column" flash chromatography (95:5 hexane–ethyl acetate) 0.122 g (61%) of 1,1,1-trichloro-5-hexen-2-one (**7a**) as a colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 5.9–5.7 (1 H, m), 5.2–5.0 (2 H, m), 3.11 (2 H, t, *J* = 7.2 Hz), 2.5–2.4 (2 H, m); IR (film) 3080, 2920, 2860, 1755, 1640, 1440, 1410, 1355, 1125, 1080, 1000, 920, 840, 800, 755, 695 cm^{-1}.

1,1,1-Trichloro-6-hepten-2-one (7b). **7b** was prepared in a manner similar to that described for 1,1,1-trichloro-5-hexen-2-one (**7a**). 1,1,1-Trichloro-6-hepten-2-ol (**5b**; 1.0 g, 4.6 mmol) was oxidized by Jones reagent to give after purification by "dry column" flash chromatography (97:3 hexane–ethyl acetate) and distillation [bp 45 °C (~30 Torr, bulb-to-bulb)] 0.88 g (88%) of 1,1,1-trichloro-6-hepten-2-one (**7b**) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 5.8–5.7 (1 H, m), 5.1–5.0 (2 H, m), 3.06 (2 H, t, *J* = 7.3 Hz), 2.2–2.1 (2 H, m), 1.9–1.8 (2 H, m); IR (film) 3080, 2980, 2940, 1760, 1640, 1080, 1000, 920, 860, 830, 755 cm^{-1}; ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.5, 137.1, 115.9, 96.9, 33.0, 32.6, 23.8; CIMS *m/z* 217, 215 ($M^+ + 1$), 145. Anal. Calcd for $C_7H_9Cl_3O$: C, 38.84; H, 4.19. Found: C, 38.96; H, 4.10.

***trans*-1,1,1-Trichloro-5-hepten-2-one (7c).** Chromium trioxide (1.2 g, 12 mmol) and Florisil (~10 g) were added to a solution of pyridine (1.9 g, 24 mmol) and 25 mL of methylene chloride at −18 °C. The solution was warmed to room temperature and stirred for 0.5 h. The solution was recooled to −18 °C, and *trans*-1,1,1-trichloro-5-hepten-2-ol (**5c**; 0.40 g, 1.8 mmol) in 4 mL of methylene chloride was added dropwise. The reaction mixture was warmed to room temperature and stirred for 3 h. The crude mixture was diluted with 50 mL of ether and filtered through Florisil. The eluent was extracted with 5% HCl and brine, dried over sodium sulfate, and purified by flash chromatography (9:1, hexane–ethyl acetate) to give 0.24 g (60%) of *trans*-1,1,1-trichloro-5-hepten-2-one (**7c**) as a colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 5.6–5.2 (2 H, m), 3.03 (2 H, t, *J* = 7.2 Hz), 2.4–2.3 (2 H, m), 1.63 (3 H, d, *J* = 5.9 Hz); IR (film) 3020, 2970, 2930, 2860, 1760, 1450, 1090, 980, 845, 810, 760, 710 cm^{-1}; ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.4, 128.1, 127.1, 96.3, 33.9, 27.6, 17.0; CIMS *m/z* 217, 215 ($M^+ + 1$).

General Procedure for Metal-Catalyzed Kharasch Cyclizations. The chloro olefin (~0.3 mmol) and transition-metal catalyst were placed in a resealable Pyrex tube, and 1.0 mL of benzene was added. The mixture was degassed via three freeze/thaw cycles. The tube was sealed under vacuum, placed in an oil bath, and heated at 155–160 °C for several hours. After cooling to room temperature, the vessel was opened under argon. A small aliquot was passed through a Florisil plug and was analyzed by GLC to determine if the reaction was complete. If the starting trichloroalkene remained, the solution was degassed again and heated as before. Once the reaction was complete, hexane (3 mL) was added to the solution and the mixture was filtered through a 3-cm Florisil plug, which was eluted with benzene, and the solvent was removed in vacuo. Crude product mixtures were analyzed by GLC (see Table I, eqs 2–5).

Cyclization of Trichloroalkene 1. Products from cyclization of 1,1,1-trichloro-5-hexene (1) by the method described above were isolated by HPLC (hexane). Data for these compounds are given below.

2-(Chloromethyl)-1,1-dichlorocyclopentane (8): ^1H NMR (200 MHz, $CDCl_3$) δ 3.98 (1 H, dd, *J* = 3.9, 10.8 Hz), 3.55 (1 H, dd, *J* = 10.1, 10.4 Hz), 2.7–2.6 (2 H, m), 2.50 (1 H, dt, *J* = 10.9, 13.8 Hz), 2.3–2.2 (1 H, m), 2.0–1.5 (3 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 93.4, 57.4, 48.4, 44.3, 27.3, 19.8; IR (film) 2960, 2880, 1450, 1320, 1260, 1210, 1020, 970, 890, 750 cm^{-1}.

1,1,3-Trichlorocyclohexane (9): ^1H NMR (200 MHz, $CDCl_3$) δ 4.11 (1 H, tt, *J* = 4.2, 11.6 Hz), 3.1–3.0 (1 H, m), 2.6–2.5 (1 H,

m), 2.5–1.5 (6 H, m); IR (film) 2960, 2920, 2870, 1450, 1260, 1230, 1120, 1040, 990, 915, 890, 850, 770, 730 cm^{-1}.

Cyclization of Trichloroalkene 2. Pure chlorocyclohexane **10** and -cycloheptane **11** were isolated from the cyclization of 1,1,1-trichloro-6-heptene (**2**) by preparative TLC (hexane). Data for the pure products are reported below.

2-(Chloromethyl)-1,1-dichlorocyclohexane (10): ^1H NMR (200 MHz, $CDCl_3$) δ 4.23 (1 H, dd, J = 2.4, 10.9 Hz), 3.41 (1 H, dd, J = 9.8, 10.8 Hz), 2.7–2.6 (1 H, m), 2.3–2.1 (3 H, m), 1.9–1.6 (3 H, m), 1.6–1.3 (2 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 94.1, 54.8, 47.6, 45.6, 27.3, 24.4, 23.8; IR (film) 2950, 2870, 1450, 1270, 1260, 1140, 1120, 1100, 970, 930, 890, 870, 820, 800, 760, 740 cm^{-1}; MS m/z (relative intensity) 202 (0.1), 200 (0.1), 167 (15), 165 (23).

1,1,3-Trichlorocycloheptane (11): ^1H NMR (360 MHz, $CDCl_3$) δ 4.3–4.1 (1 H, m), 3.24 (1 H, dd, J = 1.3, 14.9 Hz), 2.86 (1 H, dd, J = 10.4, 14.9 Hz), 2.6–2.5 (2 H, m), 2.3 (1 H, m), 2.0–1.9 (1 H, m), 1.8–1.6 (4 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 90.7, 58.5, 55.8, 49.7, 38.4, 24.8, 23.1; IR (film) 2940, 2870, 1455, 1270, 1020, 810 cm^{-1}.

Cyclization of Trichloroalkene 3. Using the general procedure for the cyclization, 54 mg (0.24 mmol) of trichloroalkene **3** was treated with 12 mg (0.013 mmol) of $RuCl_2(PPh_3)_3$ for 39 h to give 54 mg of crude product, which GLC indicated consisted of a 93% yield of fused chloroalkane **14**. Pure **14** was obtained by HPLC (hexane): ^1H NMR (300 MHz, $CDCl_3$) δ 4.7–4.6 (1 H, m), 2.8 (1 H, dd, J = 3.4, 9.6 Hz), 2.68 (1 H, ddd, J = 2.8, 8.3, 14 Hz), 2.6–2.4 (2 H, m), 2.3–2.2 (2 H, m), 2.2–1.9 (1 H, m), 1.8–1.4 (5 H, m); IR (film) 2950, 2880, 1460, 1240, 1215, 1020, 995, 930, 900, 880, 835, 760, 640 cm^{-1}; ^{13}C NMR (75 MHz, $CDCl_3$) δ 92.7, 60.9, 56.8, 48.0, 33.6, 32.1, 29.4, 28.6, 19.1; MS m/z (relative intensity) 228 (0.3), 226 (0.3), 155 (100), 79 (41); exact mass calcd for $C_9H_{13}Cl_3$ 226.0083, found 226.0092.

Cyclization of Trichloro Alcohol 5a. Using the general procedure for cyclization, trichloro alcohol **5a** was isomerized to a diastereomeric mixture of cyclopentyl alcohols **12** and cyclohexyl alcohol **13**. These products were isolated by HPLC (85:15, hexane–ethyl acetate), and data for these compounds are listed below:

3-(Chloromethyl)-2,2-dichlorocyclopentanol (12). Major isomer: ^1H NMR (360 MHz, $CDCl_3$) δ 4.3 (1 H, m), 3.96 (1 H, dd, J = 4.1, 10.7 Hz), 3.62 (1 H, dd, J = 10.0, 10.7 Hz), 3.1–2.9 (1 H, m), 2.59 (1 H, s), 2.4–2.2 (2 H, m), 2.0–1.6 (2 H, m); IR (film) 3420, 2960, 2880, 1460, 1445, 1320, 1210, 1080, 1040, 1005, 930, 895, 825, 730 cm^{-1}; MS m/z (relative intensity) 204 (4.6), 202 (4.7), 57 (100); exact mass calcd for $C_6H_9OCl_3$ 201.9719, found 201.9723.

Minor isomer: ^1H NMR (360 MHz, $CDCl_3$) δ 4.4–4.2 (1 H, m), 4.00 (1 H, dd, J = 4.0, 10.8 Hz), 3.61 (1 H, dd, J = 10.1, 10.7 Hz), 2.8–2.7 (1 H, m), 2.31 (1 H, d, J = 8.3 Hz), 2.3–2.1 (2 H, m), 1.8–1.6 (2 H, m); IR (film) 3400, 2980, 2960, 2880, 1460, 1450, 1405, 1305, 1365, 1135, 1120, 1080, 955, 910, 875, 840, 770, 745 cm^{-1}; MS m/z (relative intensity) 204 (4.8), 202 (5.0), 57 (100); exact mass calcd for $C_6H_9OCl_3$ 201.7919, found 201.9724.

2,2,4-Trichlorocyclohexanol (13): ^1H NMR (360 MHz, $CDCl_3$) δ 4.1 (1 H, m), 3.9–3.8 (1 H, m), 3.2–3.1 (1 H, m), 2.5–2.4 (2 H, m), 2.2–1.8 (2 H, m), 1.7–1.6 (2 H, m); IR (film) 3400, 2960, 2870, 1450, 1220, 1120, 1065, 1050, 970, 905, 880, 850, 765, 750 cm^{-1}.

Cyclization of Unsaturated Trichloro TBDMS Ether 6. Using the general procedure for cyclization, trichloro TBDMS ether **6** was cyclized and deprotected by addition of 1.6 equiv of Bu_4NF to the crude reaction mixture. Spectral data for the cyclization products **12** and **13** are given above.

Cyclization of 1,1,1-Trichloro-5-hexen-2-one (7a). Using the general procedure for cyclization, trichloro ketone **7a** was isomerized to cyclohexanone **17** and cyclopentanone **18**, which were isolated by HPLC (85:15, hexane–ethyl acetate). Spectral data for these compounds are listed below.

2,2,4-Trichlorocyclohexanone (17): ^1H NMR (300 MHz, $CDCl_3$) δ 4.47 (1 H, tt, J = 4, 12 Hz), 3.32 (1 H, dt, J = 4, 15 Hz), 3.14 (1 H, dt, J = 6, 15 Hz), 2.76 (1 H, dd, J = 11.4, 14.4 Hz), 2.66 (1 H, ddd, J = 2.8, 4.6, 15 Hz), 2.6–2.4 (1 H, m), 2.2–2.0 (1 H, m); IR (film) 2970, 2920, 1750, 1440, 1250, 1230, 1145, 1100, 1080, 985, 920, 890, 815, 785, 750 cm^{-1}; MS m/z (relative intensity) 202 (15), 200 (13), 57 (83), 55 (100), 49 (47).

3-(Chloromethyl)-2,2-dichlorocyclopentanone (18): ^1H NMR (360 MHz, $CDCl_3$) δ 4.04 (1 H, dd, J = 4.2, 11.2 Hz), 3.69 (1 H, dd, J = 9.4, 11.2 Hz), 2.8–2.7 (2 H, m), 2.5–2.4 (2 H, m), 1.9–1.8 (1 H, m); IR (film) 2930, 1760, 1155, 1130, 1090, 1070, 930, 900, 875, 825, 770, 725, 610 cm^{-1}.

Cyclization of *trans*-1,1,1-Trichloro-5-hepten-2-one (7c). *trans*-1,1,1-Trichloro-5-hepten-2-one (**7c**) was cyclized by the standard reaction conditions to give *cis*-2,2,4-trichloro-3-methylcyclohexanone (**19**) and *trans*-2,2,4-trichloro-3-methylcyclohexanone (**20**). The major cyclization product **19** could be purified by HPLC (9:1, hexane–ethyl acetate). The minor product **20** could not be obtained in pure form.

***cis*-3-Methyl-2,2,4-trichlorocyclohexanone (19):** ^1H NMR (300 MHz, $CDCl_3$) δ 4.04 (1 H, ddd, J = 4.3, 10.6, 12.0 Hz), 3.21 (1 H, td, J = 6.0, 14.9 Hz), 2.65 (1 H, ddd, J = 2.7, 4.6, 14.8 Hz), 2.6–2.5 (1 H, m), 2.46 (1 H, dq, J = 6.3, 10.6 Hz), 2.1–2.0 (1 H, m), 1.62 (3 H, d, J = 6.3 Hz); IR (film) 2990, 2920, 2880, 1750, 1455, 1430, 1380, 1250, 1220, 1200, 1155, 1095, 875, 815, 770, 725, 700, 660 cm^{-1}; CIMS m/z 217, 215 ($M^+ + 1$).

Cyclization of 1,1,1-Trichloro-6-hepten-2-one (7b). Using the general cyclization procedure, 1,1,1-trichloro-6-hepten-2-one (**7b**) was isomerized to cyclohexanone **21** and cycloheptanone **22**, and these compounds were purified by HPLC (85:15, hexane–ethyl acetate). The data for these cyclization products are listed below.

3-(Chloromethyl)-2,2-dichlorocyclohexanone (21): ^1H NMR (200 MHz, $CDCl_3$) δ 4.19 (1 H, dd, J = 2.7, 11 Hz), 3.61 (1 H, dd, J = 9.8, 11 Hz), 3.2–3.0 (1 H, m), 2.7–2.4 (3 H, m), 2.2–2.1 (1 H, m), 1.8–1.6 (2 H, m); IR (film) 2970, 2880, 1750, 1450, 1425, 1210, 1160, 1115, 1040, 970, 850, 815, 785, 740 cm^{-1}; MS m/z (relative intensity) 216 (11), 214 (12), 55 (100), 39 (40); exact mass calcd for $C_7H_9OCl_3$ 213.9719, found 213.9726.

2,2,4-Trichlorocycloheptanone (22): ^1H NMR (360 MHz, $CDCl_3$) δ 4.1–4.0 (1 H, m), 3.4–3.3 (1 H, m), 2.9–2.8 (3 H, m), 2.4–2.3 (1 H, m), 2.2–2.1 (1 H, m), 1.9–1.7 (2 H, m); IR (film) 2960, 2880, 1745, 1455, 1165, 1140, 990, 920, 825, 745, 680 cm^{-1}; MS m/z (relative intensity) 216 (6.1), 214 (6.4), 83 (49), 55 (100); exact mass calcd for $C_7H_9OCl_3$ 213.9719, found 213.9727.

Acknowledgment. This work was supported by the National Institutes of Health (Grant GM 32299).

Registry No. **1**, 124604-20-2; **2**, 32767-78-5; **3**, 124604-21-3; **4a**, 2100-17-6; **4b**, 764-59-0; **4c**, 25166-87-4; **5a**, 124604-22-4; **5b**, 124604-37-1; **5c**, 124604-38-2; **6**, 124604-23-5; **7a**, 124604-24-6; **7b**, 124604-39-3; **7c**, 124604-40-6; **8**, 124604-25-7; **9**, 124604-26-8; **10**, 124604-27-9; **11**, 124604-28-0; *cis*-**12**, 124604-29-1; *trans*-**12**, 124604-41-7; **13**, 124604-30-4; (3aα,7α,7aα)-**14**, 124604-31-5; (3aα,7β,7aα)-**14**, 124604-42-8; **15**, 68031-44-7; **16**, 124604-32-6; **17**, 32025-24-4; **18**, 124604-33-7; **19**, 124618-69-5; **20**, 124604-34-8; **21**, 124604-35-9; **22**, 124604-36-0; $CHCl_3$, 67-66-3; $I(CH_2)_3CH{=}CH_2$, 7766-48-5; $I(CH_2)_4CH{=}CH_2$, 18922-04-8; $RuCl_2(PPh_3)_3$, 15529-49-4; $FeCl_2[P(OEt)_3]$, 70317-95-2; $[CpMo(CO)_3]_2$, 12091-64-4; 2-(2-cyclohexyl)-1-iodoethane, 119867-25-3.