a range of conditions. The first-order plots of the rate data measured in the high THF concentration limit (greater than 7.3 M) are reasonably linear to only 2.0 half-lives. Beyond 75% conversion, competitive elimination causes a distinct upward curvature whereas a measured fractional order causes downward curvature (see text). Various corrections of the raw kinetic data to account for the elimination pathway causes the calculated values of k_{obsd} to increase by up to 15%, and yet the calculated orders in *n*-butyl bromide and THF remain relatively unaffected. Hence, the reported pseudo-first-order rate constants were calculated from uncorrected raw data. The linear and nonlinear least-squares numerical fits were carried out with the LTPLOT statistical package developed within the Material Sciences Center at Cornell University.

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Registry No. BuBr, 109-65-9; Ph_2NLi, 5856-89-3; LiBr, 7550-35-8; *n*-octyl bromide, 111-83-1.

Exploratory Studies of the Transition Metal Catalyzed Intramolecular Cyclization of Unsaturated α,α-Dichloro Esters, Acids, and Nitriles[1]

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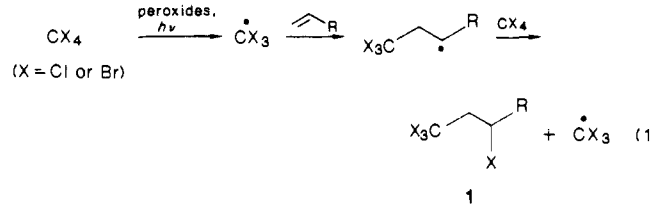
Abstract: A general method for the synthesis of functionalized carbocyclic ring systems has been developed on the basis of the transition metal promoted intramolecular radical cyclizations of olefinic and acetylenic dichloro compounds (Kharasch-type reactions). Catalytic amounts of Ru or Fe complexes were shown to generate cyclopentanes **10**, **12**, **37**, and **38**, cyclohexanes **19** and **20**, bridged systems **25**, **26**, **31**, and **32**, and fused carbocycles **34** and **35** from a variety of readily available α,α-dichloro esters **4a-f**. Several α-chloro γ-lactones, **14**, **22-24**, **27**, **33**, and **36**, could be produced by the ruthenium or iron-catalyzed cyclization of α,α-dichloro acids **5a-e** or, alternatively, directly from the esters by using a dinuclear Mo catalyst. Most reactions showed a high degree of regioselectivity in the cyclization step. Equilibration of stereoisomers via a putative α-carboxylate radical intermediate (cf. **18**, **30**) was observed in some cases. Acetylenic α,α-dichloro esters **4g,h** afforded cyclopentanoid α,β-unsaturated esters **44** and **45** via the hydrogen atom abstraction/rearrangement mechanism proposed in Scheme X. Utilizing $CuCl/PPh_3$, intramolecular ring closure of a series of olefinic α,α-dichloro-β-keto esters **6** and α,α-dichloro nitriles **9** could be carried out to yield highly functionalized carbocycles **46-56**.

An impressive array of synthetically useful methodology has recently been developed for effecting intramolecular cyclizations of carbon-centered radicals with alkenes.[2] The large preponderance of these cyclizations has been of the 5-hexenyl radical type, and most cases have involved termination of the intermediate radical by hydrogen atom abstraction. One notable exception is the manganese(III) promoted cyclization of unsaturated β-keto esters and acids, extensively studied by Corey,[3] Fristad,[4] and Snider,[5] which terminates with carbon-oxygen bond formation and thus leaves the products in a more highly functionalized state.[6] A disadvantage of this particular method is that stoichiometric amounts of metal are required.

Over 4 decades ago, Kharasch et al.[7] made the important discovery that various halocarbons will add to olefins in a radical chain process to give adducts of type **1** (eq 1).[8] A more recent advance is the observation that this addition is catalyzed by a



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number of transition-metal complexes.[9,10] A primary advantage of these metal-promoted reactions is that teleomerization is minimized in most cases. This phenomenon is presumably due to the fact that metal-coordinated radicals are intermediates, the net result being that the rate of halide abstraction becomes faster than that of teleomerization.[11]

A known variation of the Kharasch reaction utilizes trichloroacetates and related α-chloro esters (Scheme I).[12] Interestingly, this addition can take two courses depending upon

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(2) For excellent reviews, see: Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon: New York, 1986. Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541.
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(6) For other exceptions, see: (a) Curran, D. P.; Chen, M.-H.; Kim, D. *J. Am. Chem. Soc.* **1986**, *108*, 2489. (b) Kraus, G. A.; Landgrebe, K. *Tetrahedron* **1985**, *41*, 4039. (c) Patel, V. F.; Pattenden, G.; Russell, J. J. *Tetrahedron Lett.* **1986**, *27*, 2303. (d) Curran, D. P.; Kim, D. *Ibid.* **1986**, *27*, 5821. (e) Curran, D. P.; Chang, C.-T. *Ibid.* **1987**, *28*, 2477.
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(9) Kochi, J. K. *Organometallic Mechanisms and Catalysis*; Academic: New York, 1978. Minisci, F.; Citterio, A. *Adv. Free-Radical Chem.* **1980**, *6*, 65.
(10) For additional lead references, see: (a) Elzinga, J.; Hogeveen, H. *J. Org. Chem.* **1980**, *45*, 3957. (b) Bellus, D. *Pure Appl. Chem.* **1985**, *57*, 1827. (c) Grigg, R.; Devlin, J.; Ramasubbu, A.; Scott, R. M.; Stevenson, P. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1515. (d) Martin, P.; Steiner, E.; Streith, J.; Winkler, T.; Bellus, D. *Tetrahedron* **1985**, *41*, 4057. (e) Tsuji, J.; Sato, K.; Nagashima, H. *Tetrahedron* **1985**, *41*, 5003. (f) Freidlina, R. K.; Velichko, F. K. *Synthesis* **1977**, 145.
(11) Recent mechanistic studies: 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. *Ibid.* **1984**, *267*, C45.
(12) (a) Murai, S.; Sonoda, N.; Tsutsumi, S. *J. Org. Chem.* **1964**, *29*, 2104. (b) Mori, Y.; Tsuji, J. *Tetrahedron* **1972**, *28*, 29. (c) Matsumoto, H.; Nikaido, T.; Nagai, Y. *J. Org. Chem.* **1976**, *41*, 396.

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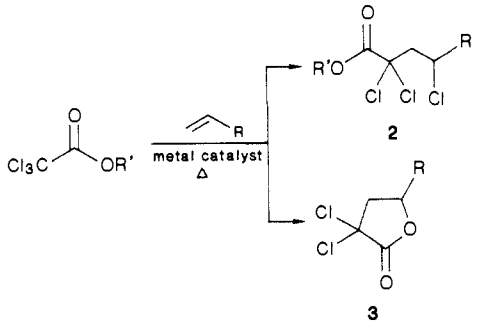
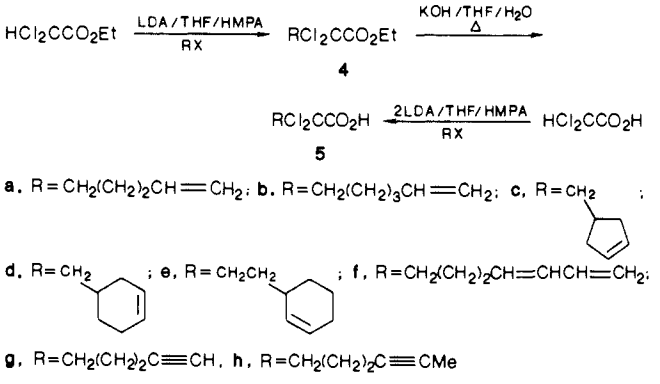
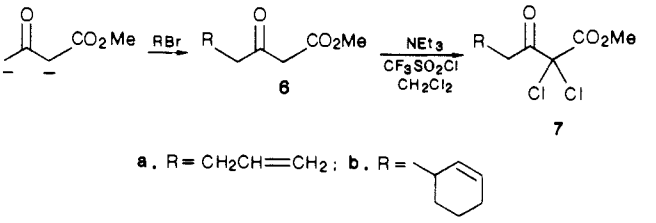
Scheme I



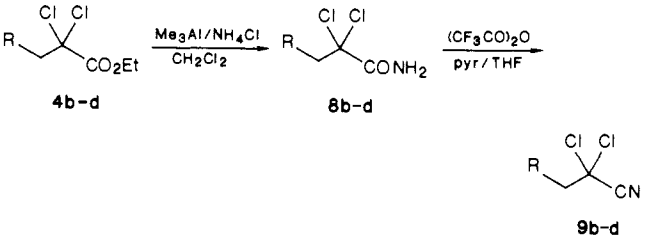
Scheme II



Scheme III

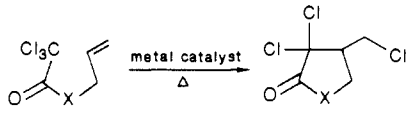


Scheme IV



which trichloroacetate substrate and metal catalyst are used. Thus, in some cases trichloro ester **2** is produced,[12] whereas in other additions the dichloro γ-lactone **3** is the product.[12b,13] For example, with ethyl trichloroacetate and Cu^+, Ru^{2+} or $Co_2(CO)_8$ as catalyst, trichloro ester addition products **2** are formed,[12] while with $[CpMo(CO)_3]_2$ and $[CpFe(CO)_2]_2$, lactonic products **3** are preferred. If trichloroacetic acid or its silyl ester are used as the halocarbon substrate, and Ru^{2+} is the catalyst, γ-lactones **3** are produced.[13]

A few publications have appeared that describe intramolecular cyclizations of allylic trichloroacetates[14] and trichloroacetamides[15] to produce trichloro γ-lactones and lactams, respectively (eq 2). These transformations are generally promoted by Cu^+ or Ru^{2+} complexes.



(2)

X = O, NR

We have recently become interested in exploring the possibility of using the metal-catalyzed Kharasch reaction in an intramolecular sense to generate highly functionalized carbocyclic systems.[1] Since product formation in a Kharasch reaction involves halogen atom abstraction, the cyclization adducts would be in a higher oxidation state than those from the more common hydrogen atom terminated radical reactions alluded to above, which involve hydrogen atom abstraction as the ultimate step.

Preparation of Cyclization Substrates. The halogenated substrates needed for the planned cyclization studies could be readily prepared by known, straightforward methodology. α,α-Dichloro esters **4a–h** and dichloro acids **5a–h** were synthesized as outlined in Scheme II. Several esters **4** were made by alkylation of the lithium enolate of ethyl dichloroacetate[16] with the appropriate primary alkyl bromide or iodide.[17] Similarly, alkylation of the dianion of dichloroacetic acid[18] afforded the acids **5**. In some cases it was more convenient to prepare the acids by saponification of the esters (see the Experimental Section).

Another series of dichlorinated carbonyl compounds was generated as shown in Scheme III. Dilithiomethyl acetoacetate was alkylated to give β-keto esters **6a,b**,[19] which were dichlorinated with triflic chloride to give α,α-dichloro-β-keto esters **7a,b**.[20]

Since we were unable to directly C-alkylate the anion of dichloroacetonitrile, the α,α-dichloro nitriles used in this study were synthesized from the corresponding esters as shown in Scheme IV. Conversion of esters **4b–d** to the amides **8b–d** was effected with the aluminum amide reagent generated from trimethylaluminum and ammonium chloride.[21] Dehydration of these amides with trifluoroacetic anhydride[22] yielded nitriles **9b–d**.

Cyclization Studies. A number of detailed preliminary experiments designed to test the feasibility of the methodology were run with α,α-dichloro carboxyl substrates **4a** and **5a**. These initial studies were intended to determine (1) which organometallic catalysts would be effective in promoting the cyclization and (2) what factors would control whether chloro ester adducts of type **2** or chloro γ-lactones such as **3** are produced. We were also interested in probing stereochemical issues related to the cyclization chemistry.

Some representative cyclizations of ester **4a** are shown in Table I. The reactions listed in this table were conducted at 155–160 °C in benzene (sealed tube), but similar results could be obtained in refluxing *tert*-butylbenzene. In refluxing xylene, the rate of cyclization was somewhat slower. With $RuCl_2(PPh_3)_3$ as catalyst (entries 1–5), the cyclopentanoid esters **10** and **12** were obtained in ratios that were highly dependent upon catalyst concentration and reaction time. These products, which are derived from exo closure of a putative intermediate metal coordinated 5-hexenyl radical,[11] were accompanied by a small amount of the cyclohexyl products **15**,[23] resulting from endo cyclization.[24] Dichloro ester

(13) (a) Matsumoto, H.; Nakano, T.; Ohkawa, K.; Nagai, Y. *Chem. Lett.* **1978**, 363. (b) Matsumoto, H.; Ohkawa, K.; Ikemori, S.; Nakano, T.; Nagai, Y. *Ibid.* **1979**, 1011.

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(16) Villieras, J.; Disnar, J. R.; Perriot, P.; Normant, J. F. *Synthesis* **1975**, 524.

(17) Iodides were prepared from the corresponding alcohols by the method of Elliot, W. J.; Fried, J. *J. Org. Chem.* **1976**, *41*, 2475.

(18) Coutrot, P.; El Gadi, A. *Synthesis* **1984**, 115.

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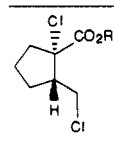
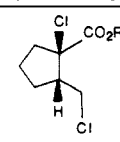
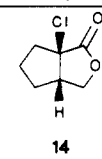
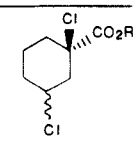
(21) Levin, J. I.; Turos, E.; Weinreb, S. M. *Synth. Commun.* **1982**, *12*, 989.

(22) Campagna, F.; Carotti, A.; Casini, G. *Tetrahedron Lett.* **1977**, 1813.

(23) These minor isomers were not identified in our earlier published work.[1]

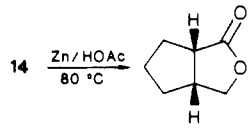
(24) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073. Giese, B. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 553.

Table I. Cyclization of α,α-Dichloro Ester **4a** and Acid **5a**[a]

					cyclization products, % yield[b]			
								
					10, R=Et	**12**, R=Et		**15**, R=Et
entry	substrate	catalyst	mol %	time, h	**11**[d], R=H	**13**[d], R=H	**14**	**16**[d], R=H
1	**4a**	$RuCl_2(PPh_3)_3$	3.1	7	41	36		5
2		$RuCl_2(PPh_3)_3$	3.0	16	49	12		3
3		$RuCl_2(PPh_3)_3$	4.2	18	38	37		5
4		$RuCl_2(PPh_3)_3$	8.3	22	61	13		6
5		$RuCl_2(PPh_3)_3$	2.0	40	39	38		5
6		$FeCl_2[P(OEt)_3]_3$	5.7	8	51	24		5
7		$FeCl_2[P(OEt)_3]_3$	12	16	44	12	6	5
8		$FeCl_2[P(OEt)_3]_3$	3.7	20	53	10		7
9		$FeCl_2[P(OEt)_3]_3$	5.6	30	26	45		3
10		$FeCl_2[P(OEt)_3]_3$	4.2	40	48	11	4	5
11		$FeCl_2/P(OEt)_3$[c]	12	12	46	26	14	9
12		$[CpMo(CO)_3]_2$	5.5	8	10	2	50	7
13	**5a**	$RuCl_2(PPh_3)_3$	1.9	7			94	4
14		$FeCl_2[P(OEt)_3]_3$	4.0	24			66	6
15		$[CpMo(CO)_3]_2$	1.8	6	2	2	34	5

[a] Reactions were run in benzene at 155–160 °C (see the Experimental Section). [b] Yields determined by GLC. All compounds were isolated in pure form and were characterized spectrally. [c] Catalyst generated in situ. [d] Compounds **11**, **13**, and **16** were treated with excess CH_2N_2 before GLC analysis.

15 was predominantly one isomer, but its stereochemistry was not established. The stereochemical assignments of **10** and **12** are based upon the fact that the latter compound cyclized to lactone **14** with $AgNO_3$,[25] whereas the former was unreactive under the same conditions. The structure of lactone **14** was confirmed by zinc reduction to the known lactone **17** (eq 3).[6b]

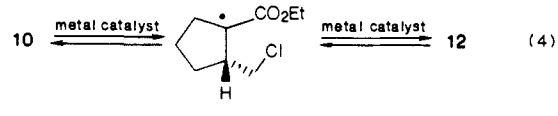


(3)

17

Another excellent and very inexpensive cyclization catalyst is $FeCl_2[(EtO)_3P]_3$,[26] which could either be prepared and used in pure form (entries 6–10) or generated in situ (entry 11). Results with this iron system were similar to those with ruthenium, although small amounts of lactone **14** were occasionally detected. Ferrous chloride or triethyl phosphite alone do not catalyze the cyclization. With $[CpMo(CO)_3]_2$ lactone **14** was in fact the major cyclization product (entry 12), a result in accord with previous observations in intermolecular reactions of trichloro- and dichloroacetates.[12]

If the cyclization reactions of α,α-dichloro ester **4a** are monitored by GLC, one sees that isomer **12** is rapidly formed. As the reaction progresses, **12** slowly decreases and epimeric isomer **10** increases. We believe that this equilibration occurs via reversible formation of ester radical **18** (eq 4). This postulate is



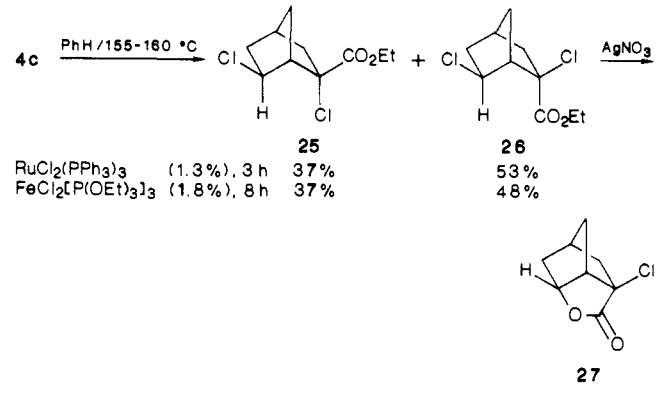
(4)

18

compatible with the results discussed below and with the fact that unsaturated α-monochloro esters undergo radical cyclizations analogous to **4a**.[27]

Several attempts were made to equilibrate purified samples of α,α-dichloro esters **10** and **12** with various transition-metal catalysts. However, the results of these experiments were not reproducible. Davis et al.[11] have found in their mechanistic studies of the metal promoted intermolecular Kharasch reaction that decomposition products of the original organometallic catalyst affect the reaction kinetics. It is conceivable that formation of radical **18** from **10** and **12** may also be influenced by these decomposition products.

Scheme V



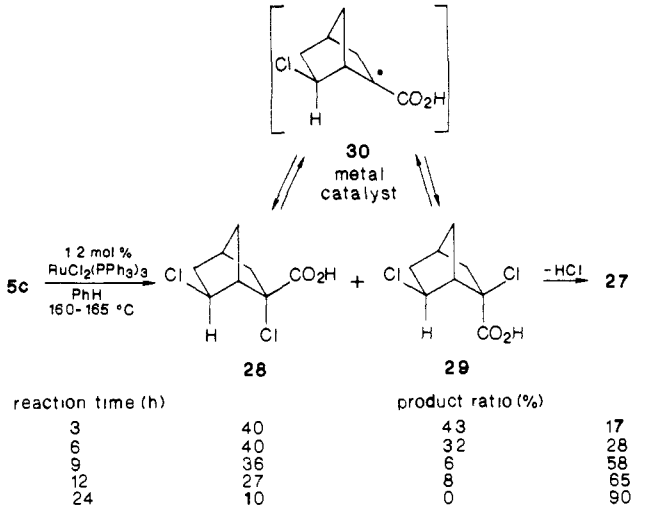
Cyclization of α,α-dichloro ester **4a** could not be effected with $NiCl_2(PPh_3)_3$,[28] $Co_2(CO)_8$,[29] or $CuCl(PPh_3)$. Cyclization occurred only slowly with $CuCl/NEt_3/MeCN$[19d] as catalyst. With $[CpFe(CO)_2]_2$ results were similar to those with the binuclear molybdenum catalyst.[12b]

As we had anticipated on the basis of the report of Matsumoto et al.,[13b] α,α-dichloro acid **5a** cyclized cleanly with both the ruthenium (entry 13) and iron (entry 14) catalysts to afford a *cis*-α-chloro γ-lactone **14** as the primary product (Table I). Interestingly, if the iron catalyst was generated in situ, the reaction of acid **50** afforded ethyl ester **4a** along with cyclized ester products **10** and **12**, but little lactone. The molybdenum catalyst also gave lactone **14** as the major product (entry 15), but yields were lower and more side products were observed. In all cases only small amounts of endo closure products **16** were found. We believe that one can best rationalize formation of cis lactone **14** from **5a** by an epimerization process as in eq 4 (vide infra).

A similar series of cyclization experiments was investigated with

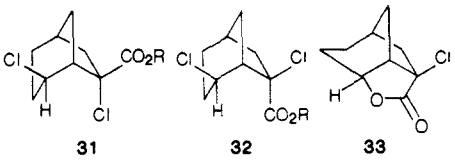
(25) Carlson, R. M.; Oyler, A. R. *J. Org. Chem.* **1976**, *41*, 4065.
(26) Ittel, S. D.; English, A. D.; Tolman, C. A.; Jesson, J. P. *Inorg. Chim. Acta* **1979**, *33*, 101. We thank Dr. W. A. Nugent (Du Pont) for bringing this catalyst to our attention.
(27) Lee, G. M.; Parvez, M.; Weinreb, S. M. *Tetrahedron*, in press.
(28) Inoue, Y.; Ohno, S.; Hashimoto, H. *Chem. Lett.* **1978**, 367.
(29) Susuki, T.; Tsuji, J. *J. Org. Chem.* **1970**, *35*, 2982.

Scheme VI



reaction time (h)	product ratio (%)		
3	40	43	17
6	40	32	28
9	36	6	58
12	27	8	65
24	10	0	90

Scheme VII



4d (R=Et)	31	32	33
$RuCl_2(PPh_3)_3$ (1.0%), 8 h	39%	44%	-
$FeCl_2[P(OEt)_3]_3$ (4.0%), 6 h	43%	48%	-
$[CpMo(CO)_3]_2$ (1.8%), 24 h	34%	2%	50%
5d (R=H)			
$RuCl_2(PPh_3)_3$ (2.1%), 8 h	1%	1%	88%
$FeCl_2[P(OEt)_3]_3$ (3.3%), 18 h	3%	-	41%
$[CpMo(CO)_3]_2$ (1.8%), 12 h	-	-	74%

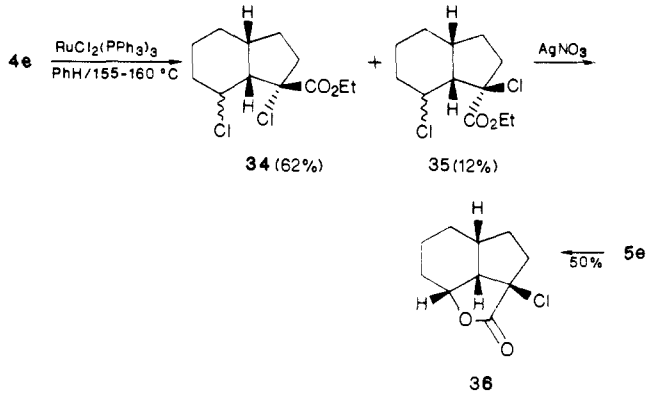
α,α-dichloro ester **4b** and acid **5b** (Table II). In these cases, although a more complex mixture of products was obtained, results were analogous to cyclizations of **4a** and **5a**. In general, the ruthenium and iron catalysts caused cyclization of ester **4b** to α,α-dichlorocyclohexanyl esters **19** and **20**, along with traces of endo closure products **21**.[23] The stereochemical assignments of **19** and **20** were based upon lactonization studies. α,γ-Dichloro ester **19** cyclized rapidly with silver nitrate[25] to cis-lactone **22**, while isomeric ester **20** cyclized very slowly to the more strained trans-fused lactone **23**. Cycloheptyl ester **21** was a mixture of major and minor stereoisomers (~7:3), which were not characterized. The molybdenum catalyst afforded a complex mixture of cyclization products **19–24**. α,α-Dichloro acid **5b** yielded lactonic products with all catalysts.

The methodology described above has also proven very useful in syntheses of bridged and fused carbocyclic systems. Treatment of ester **4c** with the ruthenium or iron catalysts gave exo [2.2.1] α,γ-dichloro ester **25** and endo compound **26** as shown in Scheme V. The stereochemistry of **26** was proven by $AgNO_3$-induced closure[25] to lactone **27**, whose structure was established by X-ray crystallography.[30] Interestingly, only *exo*-γ-Cl products were found in these reactions.

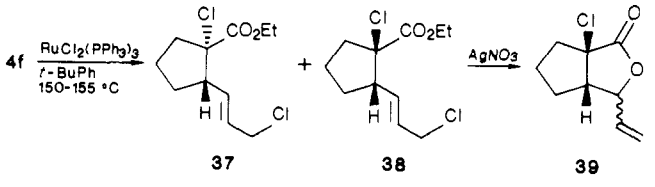
Cyclization of α,α-dichloro acid **5c** was studied in more detail. Ruthenium-promoted cyclization of **5c** was monitored by GLC, and the results are shown in Scheme VI. After a short period of time, both exo acid **28** and endo isomer **29** were formed, but only minor amounts of lactone **27** were detectable. As the reaction progressed, the amount of lactone **27** increased and *both* α,α-dichloro acids **28** and **29** disappeared. Thus, it appears that the α,γ-dichloro acids are intermediates in γ-lactone formation and that the exo isomer must be epimerizing to the endo. We propose that this happens via reversible formation of radical **30** (cf. **18**).

It was also possible to synthesize the bridged [3.2.1] systems shown in Scheme VII. α,α-Dichloro ester **4d** and acid **5d** cyclized in benzene with various catalysts in a manner analogous to systems described above. The *exo*- and *endo*-α,α-dichloro esters **31** and **32** were assigned structures on the basis of analysis of ^1H NMR data and the fact that the latter compound cyclized to lactone **33**, which was found by X-ray crystallography[30] to have the structure shown. Once again, only compounds having the exo arrangement of the γ-chlorine were produced.

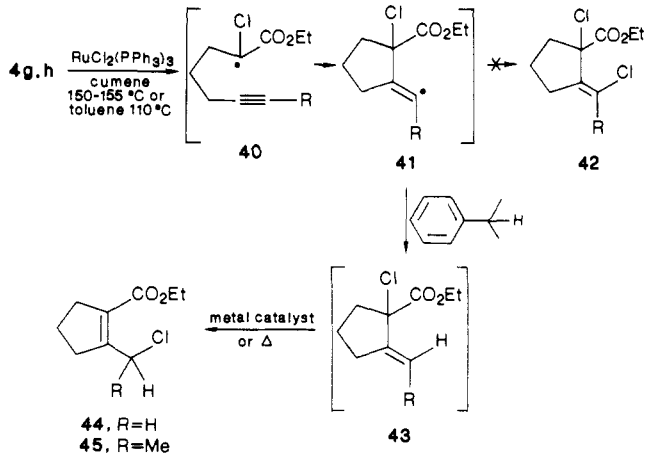
Scheme VIII



Scheme IX



Scheme X



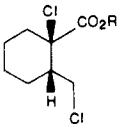
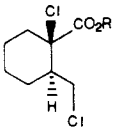
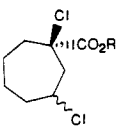
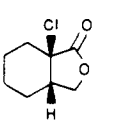
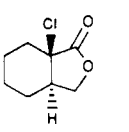
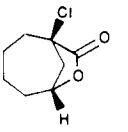
An example of a cyclization to afford a fused [6.5] ring system is shown in Scheme VIII. Ruthenium-catalyzed cyclization of α,α-dichloro ester **4e** gave two isomeric α,γ-dichloro esters **34** and **35** in good yield. The stereochemistry of **35** was correlated with lactone **36**, whose structure was determined by crystallography.[30] Cyclization product **34** does not lactonize and appears to be epimeric to **35** at the carboxylate-bearing carbon. The configuration of the γ-chlorine could not be established in either ester. α,α-Dichloro acid **5e** cyclized directly to give tricyclic α-chloro lactone **36** in 50% unoptimized yield.

We have also found that intramolecular Kharasch addition to a 1,3-diene is feasible (Scheme IX).[31] Treatment of ester **4f** with the ruthenium catalyst gave epimeric cyclization products **37** and **38** in 53% and 22% yields, respectively. Isomer **38** cyclized with silver nitrate to a separable mixture of lactones **39** while **37** was recovered unchanged. The radical closure of **4f** gave only 1,4-addition products and *E* double bond geometry, which is generally

(30) Parvez, M.; Hayes, T. K.; Weinreb, S. M. *Acta Crystallogr.*, in press.

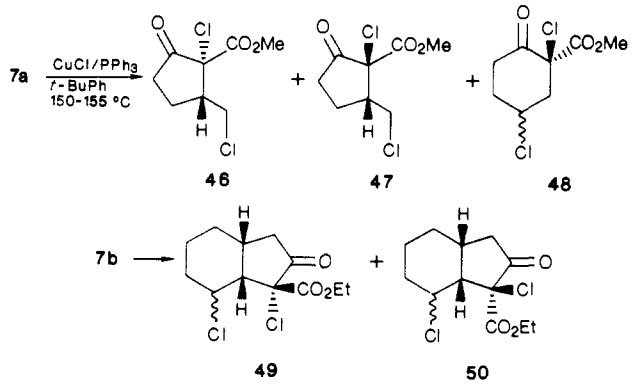
(31) For intermolecular Kharasch additions of conjugated 1,3-dienes, see: Matsumoto, H.; Nakano, T.; Nikaido, T.; Nagai, Y. *Chem. Lett.* **1978**, 115. Vit, Z.; Hajek, M. *Collect. Czech. Chem. Commun.* **1987**, *52*, 1280 and references cited therein.

Table II. Cyclization of α,α-Dichloro Ester **4b** and Acid **5b**[a]

					cyclization products, % yield[b]					
										
entry	substrate	catalyst	mol %	time, h	**19**	**20**	**21**	**22**	**23**[c]	**24**[c]
1	**4b**	$RuCl_2(PPh_3)_3$	0.8	8	20	34	7			
2		$RuCl_2(PPh_3)_3$	1.2	8	19	35	8			
3		$RuCl_2(PPh_3)_3$	1.8	24	21	24	5			
4		$RuCl_2(PPh_3)_3$	1.9	24	22	52	8			
5		$RuCl_2(PPh_3)_3$	2.5	48	19	29	9	3	3	
6		$FeCl_2[P(OEt)_3]_3$	4.2	40	23	40	4	7	11	
7		$[CpMo(CO)_3]_2$	3.3	18	7	23	6	12	23	
8	**5b**	$RuCl_2(PPh_3)_3$	3.2	24				49	40	
9		$FeCl_2[P(OEt)_3]_3$	8.2	24				35	50	
10		$[CpMo(CO)_3]_2$	3.4	40				18	17	

[a] Reactions were run in benzene at 155–160 °C (see the Experimental Section). [b] Yields determined by GLC. All compounds were isolated in pure form and were characterized spectrally. [c] Lactones **23** and **24** were not separable by GLC, but the ratio was generally about 3:7. Pure samples were isolated by HPLC (see the Experimental Section).

Scheme XI

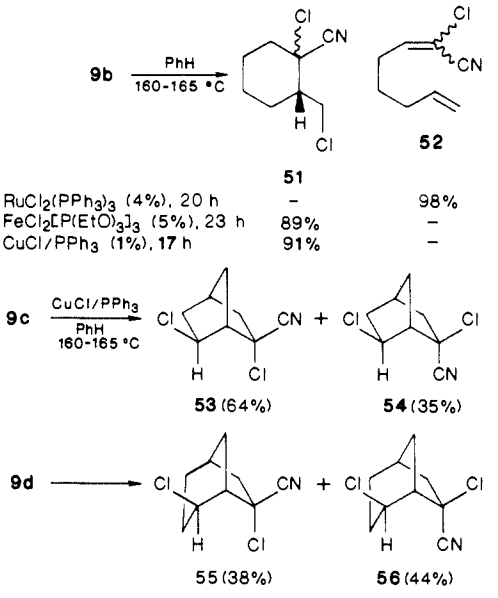


in accord with related intermolecular reactions.[31]

Intramolecular cyclizations of some α,α-dichloro ester alkynes were also briefly investigated. Heating substrate **4g** in benzene with any of the usual catalysts (Ru, Fe, Mo) gave a complex mixture of products.[32] However, if the reaction of **4g** was run in toluene or cumene with the ruthenium or iron catalysts, *none* of the Kharasch product **42** (R = H) was observed, but rather α,β-unsaturated γ-chloro ester **44** was produced in good yield (Scheme X). Similarly, alkyne α,α-dichloro ester **4h** produced cyclization product **45**. We believe that the initial radical **40**, formed from the α,α-dichloro ester, cyclizes to vinyl radical **41**, which prefers to abstract a hydrogen atom from solvent to give **43** rather than abstract chlorine to afford vinyl chloride ester **42**. In fact, when toluene was used as solvent, benzyl chloride was detected in the reaction mixture. Intermediate **43** could then rearrange via an ionic or radical process to give the observed final products **44** and **45**. Hydrogen atom abstractions by vinyl radicals in both an inter- and intramolecular sense have been observed previously in Kharasch additions to alkynes.[6a,33]

In order to expand the scope of this methodology, cyclizations of some α,α-dichloro-β-keto esters were studied, and two examples are shown in Scheme XI. Attempts to cyclize **7a** with $RuCl_2(PPh_3)_3$ or $FeCl_2[P(OEt)_3]_3$ gave only products resulting from reductive dechlorination. However, CuCl in the presence of triphenylphosphine did induce substrate **7a** to cyclize to a mixture of exo products **46** (18%), **47** (25%), and two endo cyclization products **48** (15%/9%). The amount of endo products were considerably larger than produced in cyclizations with simple esters

Scheme XII



described above. However, it should be mentioned that Curran has recently observed that α-keto radicals give more endo olefin cyclization products than do the corresponding ester radicals.[6e,34] We also noted that the ratio of products **46**/**47**/**48** formed with the copper catalyst was independent of reaction conditions and did not vary significantly with time, unlike most of the above cyclizations. It appears that this catalyst probably does not reversibly form radicals from the cyclization products, as do the ruthenium and iron catalysts (cf. eq 4).

α,α-Dichloro β-keto ester **7b** also undergoes smooth cyclization with the copper catalyst to afford **49** (10%) and **50** as a mixture of γ-chloro epimers (53%/8%). Stereochemical assignments of **49** and **50** are based upon lactonization studies (cf. Scheme VIII).

One final series of substrates that was investigated is outlined in Scheme XII. α,α-Dichloro nitriles also undergo cyclizations with various metal catalysts.[35] Since α-chloro nitriles can be hydrolyzed to ketones,[36] the overall transformation in this scheme

(32) One product that was produced in varying amounts was the ionic addition product of HCl to the alkyne group.

(33) Heiba, E. I.; Dessau, R. R. *J. Am. Chem. Soc.* **1967**, *89*, 3772. Kopchik, R. M.; Kampmeier, J. A. *Ibid.* **1968**, *90*, 6733. Haaima, G.; Weavers, R. T. *Tetrahedron Lett.* **1988**, *29*, 1085.

(34) Curran, D. P., private communication. Professor Curran has suggested that α-keto radicals in which the carbonyl group is endocyclic cyclize preferably via the endo mode for stereoelectronic reasons (cf. Clive, D. L. J.; Cheshire, D. R. *J. Chem. Soc., Chem. Commun.* **1987**, 1520).

(35) For examples of metal-catalyzed α-chloro nitrile additions to alkenes, see: Julia, M.; Le Thuillier, G.; Saussine, L. *J. Organomet. Chem.* **1979**, *177*, 221. Pews, R. G.; Lysenko, Z. *J. Org. Chem.* **1985**, *50*, 5115.

(36) Corey, E. J.; Koelliker, U.; Neuffer, J. *J. Am. Chem. Soc.* **1971**, *93*, 1489.

is equivalent to an intramolecular acyl radical/alkene addition.[37] We observed that treatment of dichloro nitrile **9b** with the ruthenium catalyst gave only HCl elimination products **52** as a mixture of E/Z isomers. However, with the ferrous chloride or cuprous chloride catalysts α,α-dichloro nitrile **51** (mixture of epimers) was produced in excellent yield. Similarly, dichloronitrile **9c** cyclized with the copper catalyst to give a mixture of norbornane epimers **53** while **54** and **9d** cyclized to yield **55** and **56**. Tentative stereochemical assignments have been made based upon spectral comparisons with compounds in Schemes V and VII.

Conclusion

In this paper we have described an efficient approach to a variety of carbocyclic systems having a high degree of functionality. The methodology works well with several different types of dichloro substrates to give both fused and bridged carbocycles. The starting α,α-dichloro esters, acids, and nitriles are easily prepared from readily available starting materials. These cyclization reactions use only catalytic amounts of transition-metal complexes and are thus inexpensive to run and avoid problems of disposal of potentially toxic metal side products. Control of product stereochemistry is possible via a presumed radical mediated equilibration, and thus in systems such as those shown in Table I and Schemes VI–VIII it is possible to drive the reaction to a single, tightly fused α-chloro γ-lactone. We are currently exploring applications of this methodology in natural product total synthesis.

Experimental Section

Melting points were measured on a Fisher–Johns apparatus and are uncorrected. Infrared spectra (IR) were recorded on a Perkin-Elmer Model 197 or Model 1310 spectrophotometer. Proton nuclear magnetic resonance spectra (^{1}H NMR) were obtained in the indicated solvents at 60 MHz on a Varian EM-360 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 50 MHz on a Bruker WP-200 instrument or at 75 MHz on a Bruker AM-300 NMR spectrometer. Low-resolution mass spectra (MS) were obtained at 50–70 eV by electron impact (EI) on a Kratos MS9/50 double-focusing mass spectrometer. Chemical ionization mass spectra (CIMS) were obtained on a Finnegan 3200 quadrupole mass spectrometer with methane or isobutane as a carrier gas. Combustion analyses were performed by Microtech Laboratories (Skokie, IL). Both analytical and preparative thin-layer chromatography (TLC) were performed with E. M. Merck silica gel PF-254. Flash and "dry-column" chromatography were done with Baker silica gel (25–40 mm) according to the procedures of Still[38] and Harwood,[39] respectively. Gas–liquid chromatography (GLC) was done on a Varian Model 3700 instrument equipped with a thermal conductivity detector and with 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 20M 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 with use of a Beckman 10 mm × 25 cm 5μ Ultrasphere column on a Waters Model 590 pump equipped with a R401 differential refractometer and a UK6 injector.

Ethyl 2,2-Dichloro-6-heptenoate (4a). Diisopropylamine (9.43 g, 13.05 mL, 93 mmol) was dissolved in 100 mL of dry THF in an oven-dried 250-mL three-necked flask equipped with an addition funnel, and the solution was cooled to −5 °C. Methyllithium (75 mL, 1.35 N, 101 mmol) was added dropwise to the mixture, and the resulting LDA solution was cooled to −55 to −60 °C. Ethyl dichloroacetate (16.00 g, 11.6 mL, 84 mmol) in 20 mL of THF was added over a period of 10–15 min.[16] After 15 min, 29.5 mL (169 mmol) of HMPA was rapidly added upon which the deep red solution changed to a dark brown. 5-Bromo-1-pentene (14.9 g, 10 mL, 84 mmol) dissolved in 20 mL of THF was slowly added over about 15 min. The temperature of the mixture was kept at −55 to −60 °C for 1 h and then allowed to rise gradually to −30 °C and maintained there for 3 h. The mixture was diluted with water (25 mL) followed by 25 mL of 5% HCl and 100 mL of Et_2O. The organic layer was washed four times with 25-mL portions of 5% HCl and once with brine and dried over $MgSO_4$. Removal of the solvent in vacuo gave a dark brown oil, which was first purified by flash chromatography, eluting with hexane/EtOAc (95:5), and then distilled to give 16.66 g (88%) of olefinic dichloro ester **4a** as a colorless liquid [bp 80–85 °C (0.5 Torr)]: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.77 (1 H, m), 5.04 (2 H, m), 4.33 (2 H, q, J = 7.1 Hz), 2.43 (2 H, m), 2.14 (2 H, m), 1.70 (2 H, m), 1.36 (3 H, t, J = 7.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.9, 137.6, 115.5, 85.2, 63.5, 44.8, 32.9, 24.6, 13.6; IR (film) 3080, 2990, 2945, 1765, 1745, 1625, 1440, 1255, 1095, 1015, 915 cm^{-1}; MS, m/z (relative intensity) 226 (0.3), 224 (0.6), 189 (14), 164 (14), 158 (65), 156 (100), 79 (42), 69 (83), 54 (79); exact mass calcd for $C_9H_{14}O_2Cl_2$ 224.0371, found 224.0373.

2,2-Dichloro-6-heptenoic Acid (5a). Diisopropylamine (3.41 g, 4.67 mL, 34 mmol) was dissolved in 50 mL of dry THF in an oven-dried 100-mL three-necked flask equipped with an addition funnel, and the solution was cooled to −5 °C. n-Butyllithium (34 mL, 1.0 N, 34 mmol) was added dropwise to the mixture, and the resulting LDA solution was cooled to −55 to −60 °C. Dichloroacetic acid (2.18 g, 1.40 mL, 17 mmol) in 10 mL of THF was added over a period of 10–15 min.[18] After 15 min, 5.90 mL (34 mmol) of HMPA was rapidly added, upon which the deep red solution changed to a dark brown. 5-Bromo-1-pentene (2.50 g, 2.00 mL, 17 mmol) dissolved in 10 mL of THF was slowly added over about 15 min. The temperature of the mixture was kept at −55 to −60 °C for 1 h and then allowed to rise gradually to −30 °C and maintained there for 3 h. The mixture was diluted with water (15 mL) followed by 15 mL of 5% HCl and 75 mL of EtOAc. The organic layer was washed four times with 25-mL portions of 5% HCl and once with brine, dried ($MgSO_4$), and concentrated to give a dark brown oil, which was first purified by flash chromatography, eluting with hexane/EtOAc (75:25), and then distilled [bp 60–65 °C (<0.1 Torr, bulb-to-bulb)] to give 2.76 g (83%) of olefinic dichloro acid **5a** as a colorless viscous oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.75 (1 H, br s, OH), 5.80 (1 H, m), 5.06 (2 H, m), 2.45 (2 H, m), 2.17 (2 H, m), 1.75 (2 H, m); IR (film) 3450, 3080, 2940, 2600, 1735, 1625, 1265, 990, 915, 445 cm^{-1}; CIMS, m/z 199, 197 (M^+ + 1), 161, 125, 81, 79. Anal. Calcd for $C_7H_{10}O_2Cl_2$: C, 42.67; H, 5.11. Found: C, 42.70; H, 5.12.

Ethyl 2,2-Dichloro-6-octenoate (4b). Following the procedure described for the preparation of dichloro ester **4a**, ethyl dichloroacetate (4.82 g, 3.50 mL, 31 mmol) was alkylated with 6-bromo-1-hexene (5.00 g, 31 mmol) to give 5.11 g (70%) of dichloro ester **4b** after purification: bp 84–88 °C (<0.1 Torr); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.77 (1 H, m), 5.04 (2 H, m), 4.33 (2 H, q, J = 7.1 Hz), 2.43 (2 H, m), 2.14 (2 H, m), 1.68–1.42 (4 H, m), 1.36 (3 H, t, J = 7.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.9, 137.6, 115.5, 85.2, 63.5, 44.8, 32.9, 24.6, 13.6; IR (film) 3080, 2990, 2945, 1765, 1745, 1625, 1255, 1095, 1015, 915 cm^{-1}; MS m/z (relative intensity) 240 (0.70), 238 (1.0), 203 (5.9), 158 (25), 156 (39), 93 (51), 68 (90), 55 (41), 41 (100), 29 (99), 28 (54). Anal. Calcd for $C_{10}H_{16}O_2Cl_2$: C, 50.23; H, 6.74. Found: C, 50.31; H, 6.86.

2,2-Dichloro-6-octenoic Acid (5b). By the application of the procedure used for the preparation of dichloro acid **5a**, dichloroacetic acid (1.84 g, 1.56 mL, 14 mmol) was alkylated with 6-iodo-1-hexene (3.00 g, 14 mmol) to give 1.89 g (70%) of dichloro acid **5b** after purification: bp 90–95 °C (<0.1 Torr, bulb-to-bulb), ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.95 (1 H, br s, OH), 5.77 (1 H, m), 5.02 (2 H, m), 2.45 (2 H, m), 2.12 (2 H, m), 1.77–1.37 (4 H, m); IR (film) 3250, 3060, 2945, 2855, 2640, 1730, 1635, 1430, 1265, 990, 910, 925, 825, 705 cm^{-1}; MS, m/z (relative intensity) 212 (0.31), 210 (0.45), 175 (5.3), 128 (26), 83 (62), 68 (74), 55 (100), 41 (88), 39 (51). Anal. Calcd for $C_8H_{12}O_2Cl_2$: C, 45.52; H, 5.73. Found: C, 45.91; H, 5.94.

Ethyl 3-(3-Cyclopentenyl)-2,2-dichloropropanoate (4c). By use of the procedure described for the preparation of dichloro ester **4a**, ethyl dichloroacetate (3.04 g, 2.25 mL, 19 mmol) was alkylated with (3-cyclopentenyl)iodomethane (4.00 g, 19 mmol) to give 4.36 g (83%) of dichloro ester **4c** after purification as above: bp 55–60 °C (0.3 Torr), ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.67 (2 H, s), 4.32 (2 H, q, J = 7.1 Hz), 2.68–2.47 (5 H, m), 2.09 (2 H, m), 1.36 (3 H, t, J = 7.1 Hz); IR (film) 3050, 2980, 2930, 2845, 1755, 1745, 1610, 1440, 1240, 1175, 1095, 1020, 690 cm^{-1}; MS, m/z (relative intensity) 238 (0.36), 236 (0.55), 200 (2.4), 81 (68), 67 (46), 66 (100), 41 (24). Anal. Calcd for $C_{10}H_{14}O_2Cl_2$: C, 50.65; H, 5.95. Found: C, 50.93; H, 6.10.

3-(3-Cyclopentenyl)-2,2-dichloropropanoic Acid (5c). Dichloro ester **4c** (3.35 g, 14 mmol) was refluxed in a solution of 20 mL of 10% KOH and 20 mL of THF for 2 h. The mixture was cooled, and 20 mL of saturated $NaHCO_3$ and 20 mL of Et_2O were added. The aqueous layer was acidified with concentrated HCl and extracted five times with CH_2Cl_2 (10-mL portions), dried ($MgSO_4$), and concentrated to a yellow oil, which gave 2.20 g (77%) of **5c** as a colorless liquid after distillation [bp 75–80 °C (<0.1 Torr, bulb-to-bulb)]; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.71 (1 H, br s, OH), 5.68 (2 H, s), 2.72–2.48 (5 H, m), 2.12 (2 H, m); IR (film) 3450, 3050, 2940, 2845, 1730, 1610, 1425, 1270, 1175, 965, 695 cm^{-1}; MS, m/z (relative intensity) 210 (0.35), 208 (0.57), 172 (12),

(37) For a recent example of acyl radical additions to alkenes, see: Coveny, D. J.; Patel, V. F.; Pattenden, G. *Tetrahedron Lett.* **1987**, *28*, 5949.
(38) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(39) Harwood, L. M. *Aldrichimica Acta* **1985**, *18*, 25.

81 (61), 67 (57), 66 (100), 41 (25); exact mass calcd for $C_8H_{10}O_2Cl_2$ 208.0058, found 208.0056.

Ethyl 3-(3-Cyclohexenyl)-2,2-dichloropropanoate (4d). Utilizing the procedure described for the preparation of dichloro ester **4a**, ethyl dichloroacetate (1.66 g, 1.20 mL, 11 mmol) was alkylated with (3-cyclohexenyl)iodomethane (2.35 g, 11 mmol) to give 1.84 g (73%) of dichloro ester **4d** after purification as above: bp 55–60 °C (0.3 Torr, bulb-to-bulb); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.56 (2 H, m), 4.26 (2 H, q, J = 7.1 Hz), 2.41 (2 H, d), 2.18–1.66 (5 H, m), 1.38 (2 H, m), 1.30 (3 H, t, J = 7.1 Hz); IR (film) 3020, 2910, 2840, 1755, 1745, 1650, 1435, 1250, 1180, 1095, 1020, 655 cm^{-1}; MS, m/z (relative intensity) 252 (2.0), 250 (3.2), 214 (5.3), 168 (13), 156 (13), 95 (96), 81 (52), 80 (100), 54 (27), 41 (23), 28 (88); exact mass calcd for $C_{11}H_{16}O_2Cl_2$ 250.0527, found 250.0534.

3-(3-Cyclohexenyl)-2,2-dichloropropanoic Acid (5d). Via the procedure used for the preparation of dichloro acid **5a**, dichloroacetic acid (2.34 g, 1.50 mL, 18 mmol) was alkylated with (3-cyclohexenyl)iodomethane (3.00 g, 14 mmol) to give 1.89 g (70%) of dichloro acid **5d** after purification as above: bp 90–95 °C (<0.1 Torr, bulb-to-bulb); ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.07 (1 H, br s, OH), 5.65 (2 H, m), 2.50 (2 H, d), 2.34–1.82 (5 H, m), 1.52–1.24 (2 H, m); IR (film) 3450, 3050, 2940, 2845, 1730, 1610, 1425, 1270, 1175, 965, 695 cm^{-1}; MS, m/z (relative intensity) 224 (1.4), 222 (2.3), 186 (3.7), 95 (100), 80 (58), 79 (39), 54 (45), 41 (23).

Ethyl 4-(2-Cyclohexenyl)-2,2-dichlorobutanoate (4e). By the application of the procedure described for the preparation of dichloroester **4a**, ethyl dichloroacetate (1.05 g, 1.45 mL, 9.1 mmol) was alkylated with 2-(2-cyclohexenyl)-1-iodoethane (2.16 g, 9.1 mmol) to give 1.47 g (61%) of dichloro ester **4e** after purification as above: bp 80–85 °C (<0.1 Torr, bulb-to-bulb); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.71 (1 H, m), 5.53 (1 H, m), 4.33 (2 H, q, J = 7.1 Hz), 2.46 (2 H, t), 2.16–1.79 (3 H, m), 1.74–1.43 (5 H, m), 1.38–1.17 (1 H, m), 1.35 (3 H, t, J = 7.1 Hz); IR (film) 3010, 2925, 2850, 1755, 1740, 1650, 1450, 1365, 1295, 1250, 1205, 1170, 1095, 1025, 865, 830, 720, 670 cm^{-1}; MS, m/z (relative intensity) 266 (0.82), 264 (1.2), 229 (7.7), 94 (100), 81 (55), 79 (36), 67 (23), 41 (28); exact mass calcd for $C_{12}H_{18}O_2Cl_2$ 264.0684, found 264.0680.

4-(2-Cyclohexenyl)-2,2-dichlorobutanoic Acid (5e). By the utilization of the saponification procedure for the preparation of dichloro acid **5c**, dichloro ester **4e** (0.311 g, 1.2 mmol) was converted to dichloro acid **5e** (0.202 g, 73%) as a yellow oil, which after flash chromatography (hexane/EtOAc, 75:25) and distillation [bp 95–110 °C (<0.1 Torr, bulb-to-bulb)] solidified in the freezer as large white crystals: mp 25–30 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.43 (1 H, br s, OH), 5.67 (1 H, m), 5.52 (1 H, m), 2.49 (2 H, t), 2.16–1.76 (3 H, m), 1.74–1.44 (5 H, m), 1.29 (1 H, m); IR (film) 3010, 2925, 2850, 1755, 1740, 1650, 1450, 1365, 1295, 1250, 1205, 1170, 1095, 1025, 865, 830, 720, 670 cm^{-1}; MS, m/z (relative intensity) 238 (3.3), 236 (5.2), 201 (4.0), 109 (29), 94 (75), 81 (100), 79 (37), 67 (30), 41 (35); exact mass calcd for $C_{10}H_{14}O_2Cl_2$ 236.0371, found 236.0373.

Ethyl 2,2-Dichloro-5,7-nonadienoate (4f). Via the procedure described for the preparation of dichloro ester **4a**, ethyl dichloroacetate (3.13 g, 2.27 mL, 20 mmol) was alkylated with 8-iodo-1,3-octadiene (4.43 g, 20 mmol) to give 3.95 g (79%) of dichloro ester **4f** after purification as above: bp 70–75 °C (<0.1 Torr, bulb-to-bulb); ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.32–5.99 (2 H, m), 5.65 (1 H, m), 5.03 (2 H, m), 4.29 (2 H, q, J = 7.1 Hz), 2.39 (2 H, m), 2.16 (2 H, m), 1.68 (2 H, m), 1.32 (3 H, t, J = 7.1 Hz); IR (film) 3090, 2990, 2945, 1760, 1750, 1655, 1605, 1460, 1375, 1260, 1105, 1015, 910, 685 cm^{-1}; MS, m/z (relative intensity) 252 (8.6), 250 (13), 215 (1.2), 156 (12), 95 (26), 80 (42), 67 (50), 41 (54), 29 (53); exact mass calcd for $C_{11}H_{16}O_2Cl_2$ 250.0527, found 250.0545.

Ethyl 2,2-Dichloro-6-heptynoate (4g). By the application of the procedure used for the preparation of dichloro ester **4a**, ethyl dichloroacetate (4.50 g, 3.26 mL, 29 mmol) was alkylated with 5-iodo-1-pentyne (5.58 g, 29 mmol) to give 4.98 g (78%) of dichloro ester **4g** after distillation: bp 78–84 °C (0.5 Torr); ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.32 (2 H, q, J = 7.1 Hz), 2.53 (2 H, m), 2.28 (2 H, m), 1.99 (1 H, t, J = 2.7 Hz), 1.82 (2 H, m), 1.34 (3 H, t, J = 7.1 Hz); IR (film) 3295, 2980, 2935, 2110, 1755, 1740, 1445, 1365, 1300, 1250, 1175, 1090, 1010, 825 cm^{-1}; CIMS, m/z 225, 223 (M$^+$ + 1). Anal. Calcd for $C_9H_{12}O_2Cl_2$: C, 48.45; H, 5.42. Found: C, 48.45; H, 5.50.

Ethyl 2,2-Dichloro-6-octynoate (4h). Via the procedure for the preparation of dichloro ester **4a**, ethyl dichloroacetate (0.73 g, 0.53 mL, 4.7 mmol) was alkylated with 6-iodo-2-hexyne (0.97 g, 4.7 mmol) to give 0.52 g (41%) of dichloro ester **4h** after purification as before: bp 50–60 °C (<0.1 Torr, bulb-to-bulb); ^{1}H NMR (200 MHz, benzene-d_6) δ 3.82 (2 H, q, J = 7.1 Hz), 2.50 (2 H, m), 1.93 (2 H, m), 1.74 (2 H, m), 1.47 (3 H, t, J = 2.5 Hz), 0.82 (3 H, t, J = 7.1 Hz); IR (film) 2970, 2930, 2905, 2850, 1755, 1740, 1450, 1295, 1210, 1175, 1090, 1015, 825 cm^{-1}; CIMS, m/z 239, 237 (M$^+$ + 1), 201.

Methyl 3-Oxo-6-heptenoate (6a).[19] *n*-Butyllithium (112 mL, 1.38 N, 154 mmol) was added dropwise over a period of 0.5 h to a cold (0 °C) solution of diisopropylamine (15.44 g, 21.5 mL, 154 mmol) in 100 mL of THF. After 20 min, 9.78 mL (10.56 g, 77 mmol) of methyl acetoacetate dissolved in 30 mL of THF was added, and the mixture was stirred for 30 min. Allyl bromide (9.31 g, 6.66 mL, 77 mmol) in 30 mL of THF was added dropwise. The reaction mixture was maintained at 0 °C for 45 min and gradually warmed to room temperature; 5% HCl (50 mL) was added, and the aqueous layer was extracted three times with 50-mL portions of Et_2O. The organic layer was backwashed once with 5% HCl and once with brine and dried ($MgSO_4$). The solvent was removed in vacuo, giving a yellow oil that was first purified by flash chromatography (hexane/EtOAc, 9:1). Distillation of the resulting oil [bp 75–80 °C (<0.1 Torr, bulb-to-bulb)] gave 8.65 g (66% yield) of **6a** as a colorless liquid: ^{1}H NMR (60 MHz, $CDCl_3$) δ 5.73 (1 H, m), 4.97 (2 H, m), 4.10 (3 H, s), 3.43 (2 H, s), 2.83–2.13 (4 H, m); IR (film) 3195, 2995, 2950, 1750, 1725, 1645, 1370, 1320, 1035, 920 cm^{-1}.

Methyl 2,2-Dichloro-3-oxo-6-heptenoate (7a).[20] The olefinic β-keto ester **6a** (1.81 g, 11 mmol) and triethylamine (2.50 g, 3.25 mL, 23 mmol) were dissolved in 25 mL of dry CH_2Cl_2, and the mixture was cooled in an ice bath. Trifluoromethanesulfonyl chloride (3.96 g, 2.50 mL, 23 mmol) was slowly added dropwise, resulting in the evolution of a dense white cloud and a slight yellowing of the solution. The reaction mixture was stirred at room temperature for 2 h, and 5% HCl (20 mL) was added. The organic phase was separated and washed three times with 20 mL of 5% HCl and once with brine and dried ($MgSO_4$). Removal of the solvent gave a yellow oil, which was purified by "dry-column" flash chromatography (hexane/EtOAc, 9:1) followed by bulb-to-bulb distillation [bp 50–65 °C (<0.1 Torr)] to give 1.92 g (75%) of **7a** as a colorless liquid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.79 (1 H, m), 5.06 (2 H, m), 3.90 (3 H, s), 2.94 (2 H, t, J = 7.3 Hz), 2.42 (2 H, m); IR (film) 3090, 2970, 2925, 1770, 1750, 1645, 1445, 1255, 1005, 925, 875 cm^{-1}; CIMS, m/z 227, 225 (M$^+$ + 1).

Methyl 4-(2-Cyclohexenyl)-3-oxobutanoate (6b). By the application of the procedure used for the preparation of β-keto ester **6a**, methyl acetoacetate (3.49 g, 3.24 mL, 30 mmol) was alkylated with 1-bromo-2-cyclohexene (4.85 g, 5.00 mL, 30 mmol) to give β-keto ester **6b**. Purification of the crude product by flash chromatography (hexane/EtOAc, 9:1) followed by distillation gave 3.41 g (77% based on 1.23 g of recovered unreacted bromide) of **6b** as a colorless oil: bp 65–75 °C (<0.1 Torr, bulb-to-bulb); ^{1}H NMR (60 MHz, $CDCl_3$) δ 5.73–5.35 (2 H, m), 3.65 (3 H, s), 3.38 (2 H, m), 2.54–1.22 (9 H, m); IR (film) 3025, 2920, 2870, 1760, 1740, 1635, 1440, 1250, 1015, 865, 735 cm^{-1}.

Methyl 4-(2-Cyclohexenyl)-2,2-dichloro-3-oxobutanoate (7b). β-Keto ester **6b** (3.41 g, 17 mmol) was chlorinated with triflic chloride (5.85 g, 3.70 mL, 35 mmol) and triethylamine (3.51 g, 4.54 mL, 35 mmol) by the procedure used for the preparation of **7a**. Flash chromatography (hexane/EtOAc, 85:15) and bulb-to-bulb distillation [bp 65–75 °C (<0.1 Torr)] of the crude product gave 3.71 g (80%) of **7b** as a colorless liquid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.72 (1 H, m), 5.49 (1 H, m), 3.90 (3 H, s), 2.83–1.72 (3 H, m), 2.03–1.55 (5 H, m), 1.26 (1 H, m); IR (film) 3010, 2930, 2860, 1770, 1740, 1435, 1360, 1260, 1115, 1010, 865, 725 cm^{-1}; CIMS, m/z 267, 265 (M$^+$ + 1), 124, 123, 122.

2,2-Dichloro-7-octenamide (8b). An aluminum amide reagent was generated by dropwise addition of 9.59 mL (19 mmol) of trimethyl aluminum (2.0 M solution in hexane) to a stirred slurry of anhydrous ammonium chloride (1.025 g, 19 mmol) in 25 mL of dry methylene chloride.[21] The mixture became homogeneous over a 20-min period. To a solution of 1.014 g (4.25 mmol) of α,α-dichloro ester **4b** in 70 mL of dry methylene chloride was added dropwise 21.2 mL (16.0 mmol) of the above aluminum amide reagent with stirring over 15 min, and the solution was refluxed under argon for 63 h. The reaction was quenched by careful addition of 40 mL of 5% HCl, and the aqueous phase was extracted three times with 70 mL of EtOAc. The combined organic phases were dried over anhydrous sodium sulfate, and the solvent was removed in vacuo. The crude product was purified by flash chromatography (hexane/EtOAc, 1:1) to give 0.804 g (95%) of the amide as a pale yellow solid: ^{1}H NMR (60 MHz, $CDCl_3$) δ 6.80 (2 H, br s, NH), 6.15–5.40 (1 H, m), 5.25–4.76 (2 H, m), 2.67–1.38 (8 H, m); IR (film) 3490, 3250, 3100, 2950, 2860, 1700, 1640, 1600, 1000, 720 cm^{-1}.

Amides **8c** and **8d** were prepared in a similar manner from the corresponding ester.

3-(3-Cyclopentenyl)-2,2-dichloropropanamide (8c): 87% yield (pale yellow solid); ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.75 (1 H, br s, NH), 6.27 (1 H, br s, NH), 5.65–5.55 (2 H, br s), 2.50 (2 H, d, J = 5.3 Hz), 2.35–1.76 (4 H, m), 1.52–1.33 (1 H, m); IR (film) 3470, 3300, 3050, 2950, 2850, 1700, 1600, 960, 860 cm^{-1}.

3-(3-Cyclohexyl)-2,2-dichloropropanamide (8d): 76% yield (yellow solid); mp 75–76 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.78 (1 H, br s, NH), 6.27 (1 H, br s, NH), 5.65–5.63 (2 H, m), 2.49 (2 H, d, J = 5.3

Hz), 2.29–1.79 (6 H, m), 1.51–1.35 (1 H, m); IR (film) 3460, 3300, 3030, 2920, 2850, 1680, 1590, 980, 700 cm^{-1}; MS, *m/z* (relative intensity) 223 (1), 221 (2), 127 (56), 95 (93), 80 (100), 44 (46); CIMS, *m/z* 226, 224, 222 ($M^+ + 1$); exact mass calcd for $C_9H_{13}OCl_2N$ 221.0374, found 221.0367.

2,2-Dichloro-7-octenenitrile (9b). A solution of amide **8b** (904 mg, 4.31 mmol) and 0.70 mL of pyridine in 70 mL of dry THF was cooled to 0 °C. To this solution was added dropwise 0.67 mL (4.74 mmol) of trifluoroacetic anhydride in 20 mL of dry THF while the temperature was maintained below 5 °C.[22] The mixture was stirred at 0 °C for 1 h, warmed to room temperature, and stirred for 3 h. Et_2O (200 mL) was added, and the organic phase was washed twice with 100 mL of H_2O and once with 100 mL of brine. The organic phase was dried over anhydrous sodium sulfate, and the solvent was removed in vacuo. The crude oily residue was purified by flash chromatography (hexane/EtOAc, 19:1) to yield a colorless oil (575 mg, 70%); ^1H NMR (200 MHz, $CDCl_3$) δ 5.91–5.70 (1 H, m), 5.11–4.98 (2 H, m), 2.53–2.45 (2 H, m), 2.33–2.05 (2 H, m), 1.83–1.68 (2 H, m), 1.66–1.44 (2 H, m); IR (film) 3100, 2950, 2850, 1640, 990, 920, 760 cm^{-1}; MS, *m/z* (relative intensity) 104 (18), 55 (90), 41 (2), 28 (100).

Nitriles **9c** and **9d** were prepared in the same fashion from the corresponding amides.

3-(3-Cyclopentenyl)-2,2-dichloropropionitrile (9c): 86% yield (colorless oil); ^1H NMR (200 MHz, $CDCl_3$) δ 5.71 (2 H, s), 2.75–2.64 (5 H, m), 2.28–2.15 (2 H, m); IR (film) 3060, 2940, 2850, 2250, 1620, 960, 760, 780 cm^{-1}; MS, *m/z* (relative intensity) 193 (1), 191 (5), 189 (7), 154 (7), 81 (63), 66 (100), 28 (16); exact mass calcd for $C_8H_9Cl_2N$ 189.0112, found 189.0113.

3-(3-Cyclohexyl)-2,2-dichloropropionitrile (9d): 83% yield (colorless oil); ^1H NMR (60 MHz, $CDCl_3$) δ 3.85–3.50 (2 H, m), 2.50 (2 H, m), 2.30–1.70 (7 H, m); IR (film) 3050, 2950, 2850, 2250, 1630, 980, 760 cm^{-1}; MS, *m/z* (relative intensity) 205 (2), 203 (3), 168 (10), 95 (100), 81 (61), 41 (49), 27 (25); exact mass calcd for $C_9H_{11}Cl_2N$ 203.0269, found 203.0277.

General Procedure for Cyclization of Unsaturated α,α-Dichloro Esters, Acids, and Nitriles. The dichloro compound 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, and the tube was sealed under vacuum, placed in an oil bath, and heated at 155–160 °C for several hours. After cooling, the vessel was opened under argon. A small aliquot was passed through a plug of Florisil and was analyzed by GLC to determine if the reaction was complete. If the starting dichloro compound remained, the solution was degassed again and heated as before. Once the reaction was complete, hexane (3 mL) and benzene (2 mL) were added to the solution, and the mixture was filtered through a 3-cm plug of Florisil, which was washed with 3 mL of benzene, and the solvent was removed in vacuo. Crude product mixtures were analyzed by GLC. Results for dichloro esters **4a** and **4b**, and dichloro acids **5a** and **5b** employing various catalysts are reported in Tables I and II.

Pure cyclic esters **10** and **12** were isolated from the cyclization of olefinic dichloro ester **4a** by using preparative TLC, eluting once with 9:1 hexane/EtOAc and once with 9:1 hexane/CH_2Cl_2. α,γ-Dichloro ester **15** could be obtained by HPLC (hexane/EtOAc, 95:5). Lactone **14** was obtained from the cyclization of olefinic dichloro acid **5a** and was purified by bulb-to-bulb distillation. Data for the purified compounds are reported below.

Ethyl *trans*-1-chloro-2-(chloromethyl)cyclopentane-1-carboxylate (10): bp 50–55 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (200 MHz, $CDCl_3$) δ 4.26 (2 H, q, *J* = 7.1 Hz), 3.82 (1 H, dd, *J* = 6.4, 11.0 Hz), 3.54 (1 H, dd, *J* = 7.8, 10.8 Hz), 2.87 (1 H, m), 2.49–1.59 (6 H, m), 1.32 (3 H, t, *J* = 7.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.5, 77.2, 62.4, 51.6, 44.8, 41.9, 28.2, 21.0, 13.9; IR (film) 2975, 2870, 1735, 1445, 1370, 1200, 1095, 1040, 920, 755 cm^{-1}; MS, *m/z* (relative intensity) 226 (1.8), 224 (2.9), 189 (51), 156 (1.4), 153 (63), 135 (34), 115 (100), 79 (94), 41 (25), 28 (91); exact mass calcd for $C_9H_{14}O_2Cl_2$ 224.0371, found 224.0372.

Heating this α,γ-dichloro ester with $AgNO_3$ in H_2O/1,4-dioxane resulted in recovery of starting material.

Ethyl *cis*-1-chloro-2-(chloromethyl)cyclopentane-1-carboxylate (12): bp 50–55 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (200 MHz, $CDCl_3$) δ 4.25 (2 H, q, *J* = 7.1 Hz), 3.71 (1 H, dd, *J* = 4.3, 10.9 Hz), 3.43 (1 H, dd, *J* = 9.1, 10.9 Hz), 2.77 (1 H, m), 2.57 (1 H, m), 2.32–1.61 (5 H, m), 1.33 (3 H, t, *J* = 7.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.5, 74.4, 62.2, 55.0, 44.6, 40.0, 28.1, 21.1, 13.9; IR (film) 2975, 2870, 1735, 1445, 1370, 1325, 1265, 1200, 1080, 1035, 1020, 915, 860, 750 cm^{-1}; MS, *m/z* (relative intensity) 226 (0.6), 224 (0.9), 189 (25), 156 (0.2), 153 (25), 135 (6), 115 (51), 79 (40), 41 (9), 28 (100); exact mass calcd for $C_9H_{14}O_2Cl_2$ 224.0371, found 224.0374.

Reaction of this compound with $AgNO_3$ in H_2O/1,4-dioxane gave lactone **14**.

Ethyl 1,3-dichlorocyclohexane-1-carboxylate (15, major): bp 50–55 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (200 MHz, $CDCl_3$) δ 4.34–4.20 (1 H, m), 4.26 (2 H, q, *J* = 7.1 Hz), 2.71 (1 H, dddd, *J* = 2.2, 2.2, 4.0, 14.0 Hz), 2.30–2.05 (3 H, m), 1.58 (1 H, m), 1.33 (3 H, t, *J* = 7.1 Hz); IR (film) 2965, 2875, 1745, 1450, 1260, 1205, 1065, 1040, 910, 760, 725 cm^{-1}; MS, *m/z* (relative intensity) 226 (1.0), 224 (2.0), 189 (13), 151 (23), 115 (100), 79 (98), 49 (41), 28 (81); exact mass calcd for $C_9H_{14}O_2Cl_2$ 224.0371, found 224.0355.

3-Chloro-1-oxabicyclo[3.3.0]octan-2-one (14): bp 90–105 °C (<0.1 Torr, bulb-to-bulb); mp 27.5–30 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 4.59 (1 H, dd, *J* = 7.0, 9.5 Hz), 4.09 (1 H, dd, *J* = 2.5, 9.5 Hz), 3.03 (1 H, m), 2.59 (1 H, m), 2.37–1.61 (5 H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.4, 71.6, 68.9, 49.1, 39.8, 31.9, 24.6; IR (film) 3510, 2975, 2880, 1785, 1480, 1445, 1380, 1205, 1150, 1005, 975, 905, 690 cm^{-1}; CIMS, *m/z* 163, 161 ($M^+ + 1$).

Pure cyclic esters **19** and **20** and epimers of **21** were isolated from the cyclization of olefinic dichloro ester **4b** by preparative HPLC, eluting with 95:5 hexane/EtOAc. Lactones **22–24** were obtained from the cyclization of olefinic dichloro acid **5b** and were isolated by HPLC (hexane/EtOAc, 95:5). Data for the purified compounds are reported below.

Ethyl *cis*-1-chloro-2-(chloromethyl)cyclohexane-1-carboxylate (19): bp 55–65 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (200 MHz, $CDCl_3$) δ 4.27 (2 H, q, *J* = 7.1 Hz), 3.58 (1 H, dd, *J* = 4.0, 11.0 Hz), 3.32 (1 H, dd, *J* = 8.9, 11.0 Hz), 2.05 (1 H, m), 1.92–1.34 (8 H, m); 1.33 (3 H, t, *J* = 7.1 Hz); IR (film) 2980, 2940, 2870, 1740, 1450, 1370, 1260, 1245, 1145, 1110, 1090, 1060, 1025, 910, 860, 740 cm^{-1}; MS, *m/z* (relative intensity) 240 (0.7), 238 (1.2), 203 (8.0), 166 (25), 130 (21), 93 (36), 84 (35), 67 (14), 49 (100); exact mass calcd for $C_{10}H_{16}O_2Cl_2$ 238.0527, found 238.0525.

Reaction of this cyclic dichloro ester with $AgNO_3$ in H_2O/1,4-dioxane gave lactone **22**.

Ethyl *trans*-1-chloro-2-(chloromethyl)cyclohexane-1-carboxylate (20): bp 55–65 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (200 MHz, $CDCl_3$) δ 4.24 (2 H, q, *J* = 7.1 Hz), 4.07 (1 H, dd, *J* = 2.1, 10.8 Hz), 3.72 (1 H, dd, *J* = 10.0, 10.8 Hz), 2.54 (1 H, m), 2.21 (2 H, m), 1.92–1.34 (6 H, m), 1.31 (3 H, t, *J* = 7.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.1, 74.3, 62.5, 46.2, 46.1, 38.2, 25.2, 24.3, 21.0, 14.0; IR (film) 2950, 2880, 1740, 1455, 1375, 1305, 1250, 1215, 1150, 1125, 1065, 1030, 980, 970, 740, 715 cm^{-1}; MS, *m/z* (relative intensity) 240 (3.0), 238 (4.6), 203 (22), 166 (35), 129 (50), 93 (100), 77 (25), 28 (66); exact mass calcd for $C_{10}H_{16}O_2Cl_2$ 238.0527, found 238.0526.

Treatment of this material with $AgNO_3$ in H_2O/1,4-dioxane resulted in slow cyclization to lactone **23**.

α,γ-Dichloro ester 21 (minor): bp 55–65 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (200 MHz, $CDCl_3$) δ 4.45–4.32 (1 H, m), 4.27 (2 H, q, *J* = 7.1 Hz), 2.84 (1 H, ddd, *J* = 1.3, 1.3, 15.2 Hz), 2.67 (1 H, dd, *J* = 10.0, 15.2 Hz), 2.46–1.54 (8 H, m), 1.32 (3 H, t, *J* = 7.1 Hz); IR (film) 2945, 2885, 1740, 1450, 1370, 1260, 1050 cm^{-1}; MS, *m/z* (relative intensity) 240 (0.5), 238 (0.8), 203 (7.8), 166 (30), 129 (43), 93 (100), 84 (27), 67 (24), 49 (45), 28 (64).

Heating this cyclic dichloro ester with $AgNO_3$ in H_2O/1,4-dioxane gave lactone **24**.

α,γ-Dichloro ester 21 (major): bp 55–65 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (200 MHz, $CDCl_3$) δ 4.29 (2 H, q, *J* = 7.1 Hz), 4.10 (1 H, m), 3.21 (1 H, ddd, *J* = 1.0, 1.1, 14.3 Hz), 2.49 (1 H, dd, *J* = 10.5, 14.3 Hz), 2.45–1.40 (8 H, m); 1.34 (3 H, t, *J* = 7.1 Hz); IR (film) 2950, 2885, 1740, 1460, 1370, 1260, 1225, 1040 cm^{-1}; MS, *m/z* (relative intensity) 240 (0.4), 238 (0.6), 203 (8.0), 166 (11), 129 (71), 93 (100), 84 (3), 67 (16), 49 (5).

Heating this α,γ-dichloro ester with $AgNO_3$ in H_2O/1,4-dioxane gave lactone **24**.

***cis*-3-Chloro-1-oxabicyclo[4.3.0]nonan-2-one (22)**: ^1H NMR (200 MHz, $CDCl_3$) δ 4.61 (1 H, dd, *J* = 4.6, 8.8 Hz), 3.97 (1 H, dd, *J* = 0.1, 8.8 Hz), 2.59 (2 H, m), 2.08–1.58 (4 H, m), 1.37–1.18 (3 H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.3, 71.0, 66.7, 44.8, 33.8, 25.5, 23.7, 22.9; IR (film) 3550, 2950, 2855, 1785, 1445, 1375, 1350, 1260, 1215, 1190, 1110, 1040, 985, 915, 850, 710, 650 cm^{-1}; CIMS, *m/z* 177, 175 ($M^+ + 1$), 149, 139, 121.

***trans*-3-Chloro-1-oxabicyclo[4.3.0]nonan-2-one (23)**: ^1H NMR (200 MHz, $CDCl_3$) δ 4.28 (1 H, dd, *J* = 6.6, 8.5 Hz), 4.18 (1 H, dd, *J* = 8.5, 10.3 Hz), 2.35–1.26 (9 H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.0, 77.4, 70.8, 47.5, 32.4, 24.2, 21.8, 20.3; IR (film) 2950, 2865, 1785, 1445, 1365, 1250, 1215, 1105, 1110, 1015, 975, 935, 730, 675 cm^{-1}.

3-Chloro-1-oxabicyclo[4.2.1]nonan-2-one (24): mp 68–70 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 4.87 (1 H, m), 2.87 (1 H, ddd, *J* = 1.7, 9.5, 12.6 Hz), 2.68 (1 H, d, *J* = 12.6 Hz), 2.42 (1 H, m), 2.23–1.49 (7 H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.3, 76.7, 65.3, 42.0, 40.8, 32.7, 23.9, 22.3; IR (film) 3550, 2950, 2930, 2860, 1785, 1470, 1455, 1365,

1215, 1155, 1120, 1000, 965, 810, 760, 740, 670 cm^{-1}; CIMS, *m/z* 177, 175 ($M^+ + 1$), 139, 121.

Lactonization of Cyclic Dichloro Ester 12 to α-Chloro γ-Lactone 14. Silver nitrate (70 mg, 0.45 mmol) was dissolved in a solution of 10 mL of H_2O and 5 mL of 1,4-dioxane, and the mixture was heated to 90 °C.[25] Ethyl *cis*-1-chloro-2-(chloromethyl)cyclopentane-1-carboxylate (**12**; 41 mg, 0.18 mmol) in 5 mL of 1,4-dioxane was added dropwise. A black solid precipitated after about 15 min. The reaction mixture was heated at 90 °C for 4 h, cooled to room temperature, and suction filtered. The 1,4-dioxane was removed in vacuo, and the aqueous residue was extracted three times with EtOAc (20-mL portions). The organic layer was washed once with brine and dried with $MgSO_4$, giving 27 mg (92%) of 3-chloro-1-oxabicyclo[3.3.0]octan-2-one (**14**) as a yellowish oil. Distillation [bp 75–85 °C (<0.1 Torr)] of the crude oil gave 22 mg (76%) of a colorless liquid, which crystallized upon being cooled in the freezer. Spectral data for this material were identical with that for the lactone obtained by the cyclization of olefinic dichloro acid **5a**.

1-Oxabicyclo[3.3.0]octan-2-one (17). A mixture of α-chloro lactone **14** (40 mg, 0.25 mmol) and 120 mg (1.8 mmol) of zinc dust in 5 mL of glacial acetic acid was heated at 80 °C in an oil bath for 8 h and cooled, and 5 mL of EtOAc was added. The mixture was suction filtered, and the filter cake washed with H_2O and EtOAc. The filtrate was washed four times with $NaHCO_3$, dried ($MgSO_4$), and concentrated to give a yellow oil. Purification of this material by preparative TLC (hexane/EtOAc, 9:1) gave 27 mg (85%) of lactone **17**: ^1H NMR (200 MHz, $CDCl_3$) δ 4.48 (1 H, dd, *J* = 7.7, 9.3 Hz), 3.99 (1 H, dd, *J* = 3.0, 9.3 Hz), 3.07–2.88 (2 H, m), 2.17–1.46 (6 H, m); IR (film) 2950, 2930, 2870, 1775, 1440, 1370, 1180, 1025, 765, 700 cm^{-1}.

Ruthenium-Promoted Cyclization of Olefinic α,α-Dichloro Ester 4c. Dichloro ester **4c** (401 mg, 1.7 mmol) was cyclized with $RuCl_2(PPh_3)_3$ (21.5 mg, 0.022 mmol) by the general method described above (6 h of heating). A yellow oil (378 mg) was obtained, which was purified on two 20 × 20 cm preparative TLC plates (hexane/EtOAc, 9:1) to give 333 mg (83%) of a colorless oil. GLC showed this material to be a mixture of endo/exo carboxylate isomers **25** and **26** in a 1.4:1 ratio. The isomers could be separated by flash chromatography, eluting with 9:1 hexane/CH_2Cl_2. Data for the purified compounds are reported below.

Ethyl *endo*,*exo*-1,3-dichlorobicyclo[2.2.1]heptane-*exo*-1-carboxylate (25): bp 65–70 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (360 MHz, $CDCl_3$) δ 4.68 (1 H, dddd, *J* = 0.8, 2.1, 3.0, 7.5 Hz), 4.26 (2 H, q, *J* = 7.1 Hz), 3.06 (1 H, br s), 2.76 (1 H, m), 2.42 (1 H, m), 2.16 (1 H, m), 1.99–1.92 (2 H, m), 1.49 (1 H, dd), 1.39 (1 H, m), 1.32 (3 H, t, *J* = 7.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.4, 85.9, 62.5, 57.1, 54.9, 43.2, 42.5, 37.0, 35.1, 13.9; IR (film) 2980, 1740, 1445, 1265, 1225, 1155, 1095, 1065 cm^{-1}; MS, *m/z* (relative intensity) 238 (0.39), 236 (0.58), 201 (15), 163 (43), 135 (43), 115 (12), 91 (100), 66 (80), 29 (69); exact mass calcd for $C_{10}H_{14}O_2Cl_2$ 236.0371, found 236.0379.

Ethyl *exo*,*exo*-1,3-dichlorobicyclo[2.2.1]heptane-*endo*-1-carboxylate (26): bp 65–70 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (360 MHz, $CDCl_3$) δ 4.28 (2 H, q, *J* = 7.1 Hz), 3.77 (1 H, dddd, *J* = 0.4, 1.8, 3.3, 7.3 Hz), 2.87 (1 H, br s), 2.47 (1 H, m), 2.39 (1 H, dd, *J* = 2.6, 14.5 Hz), 2.13–1.77 (5 H, m), 1.34 (3 H, t, *J* = 7.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.7, 70.3, 62.3, 57.9, 55.9, 43.7, 41.7, 37.2, 34.8, 14.0; IR (film) 2980, 1740, 1445, 1310, 1275, 1240, 1160, 1125, 1065, 1035 cm^{-1}; MS, *m/z* (relative intensity) 239 (0.31), 238 (0.23), 237 (0.50) ($M^+ + 1$), 236 (0.26), 201 (32), 163 (26), 135 (100), 115 (71), 91 (80), 66 (74), 29 (75).

4-Chloro-2-oxatricyclo[4.2.1.0^{4,8}]nonan-3-one (27). Cyclization of acid **5c** (286 mg, 1.4 mmol) with $RuCl_2(PPh_3)_3$ (18.2 mg, 0.019 mmol) was carried out by using the procedure for the cyclization of **4c**. Heating the mixture for 24 h gave lactone **27** as an oil, which crystallized (223 mg, 92%) after bulb-to-bulb distillation [bp 90–100 °C (<0.1 Torr)]: mp 110–115 °C (recrystallized from hexane); ^1H NMR (360 MHz, $CDCl_3$) δ 4.83 (1 H, dd, *J* = 5.5, 6.5 Hz), 3.25 (1 H, m), 2.54 (1 H, br s), 2.32 (1 H, dd, *J* = 1.9, 13.8 Hz), 2.13 (1 H, m), 1.96 (1 H, m), 1.79–1.60 (2 H, m), 1.49 (1 H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.5, 78.6, 65.0, 54.8, 46.9, 37.3, 36.5, 36.3; IR (film) 2980, 2955, 2875, 1790, 1445, 1355, 1190, 1065, 995, 885, 850, 830, 765, 690 cm^{-1}; MS, *m/z* (relative intensity) 174 (0.46), 172 (2.3), 137 (4.0), 93 (100), 77 (37), 39 (30).

Cyclization of Olefinic α,α-Dichloro Ester 4d. Via the general cyclization procedure, 170 mg (0.68 mmol) of **4d** was treated with 6.7 mg (0.007 mmol) of $RuCl_2(PPh_3)_3$ for 8 h to give 150 mg (88%) of a mixture of two major compounds (39% of **31**, 44% of **32** by GLC), which could be partially separated by preparative TLC. Data for the pure compounds are reported below.

Ethyl *endo*,*exo*-1,3-dichlorobicyclo[3.2.1]octane-*exo*-1-carboxylate (31): ^1H NMR (360 MHz, $CDCl_3$) δ 4.63 (1 H, m), 4.29 (2 H, q, *J* = 7.1 Hz), 3.11 (1 H, dd, *J* = 7.3, 15.3 Hz), 2.96 (1 H, m), 2.39–2.16 (3 H, m), 1.94–1.81 (3 H, m), 1.59–1.28 (2 H, m), 1.31 (3 H, t, *J* = 7.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.9, 71.8, 62.6, 59.6, 49.5, 41.1, 34.0, 31.8, 27.5, 27.4, 13.9; IR (film) 2950, 2860, 1740, 1440, 1255, 1205, 1175, 1115, 1055, 1030, 670 cm^{-1}; MS, *m/z* (relative intensity) 252 (1.4), 250 (2.0), 215 (22), 141 (57), 135 (58), 105 (81), 80 (100), 79 (91), 49 (25), 28 (46); exact mass calcd for $C_{11}H_{16}O_2Cl_2$ 250.0527, found 250.0513.

Ethyl *exo*,*exo*-1,3-dichlorobicyclo[4.2.1]octane-*endo*-1-carboxylate (32): ^1H NMR (200 MHz, $CDCl_3$) δ 4.42 (1 H, m), 4.24 (2 H, q, *J* = 7.1 Hz), 2.79 (1 H, m), 2.69 (1 H, d, *J* = 1.8 Hz), 2.48–2.14 (4 H, m), 1.94–1.70 (4 H, m), 1.32 (3 H, t, *J* = 7.1 Hz); IR (film) 2955, 2840, 1745, 1455, 1445, 1260, 1210, 1175, 1110, 1030, 650 cm^{-1}; MS, *m/z* (relative intensity) 252 (0.67), 250 (1.1), 215 (39), 141 (25), 135 (38), 105 (57), 80 (53), 79 (100), 49 (75), 28 (86); exact mass calcd for $C_{11}H_{16}O_2Cl_2$ 250.0527, found 250.0513.

4-Chloro-2-oxatricyclo[5.2.1.0^{4,9}]decan-3-one (33). Cyclization of the olefinic acid **5d** (214 mg, 0.97 mmol) with $RuCl_2(PPh_3)_3$ (12.6 mg, 0.013 mmol) was carried out by using the usual procedure. Heating the mixture for 24 h gave lactone **33** as an oil, which crystallized (159 mg, 88%) after bulb-to-bulb distillation [bp 70–85 °C (<0.1 Torr)]: mp 67–67.5 °C (recrystallized from hexane); ^1H NMR (360 MHz, $CDCl_3$) δ 4.91 (1 H, m), 3.14 (1 H, m), 2.52–2.38 (3 H, m), 2.08–1.56 (5 H, m), 1.29 (1 H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.9, 78.9, 68.2, 53.0, 50.4, 32.6, 28.7, 24.4, 23.1; IR (film) 2950, 2875, 1780, 1445, 1360, 1240, 1180, 1140, 1075, 990, 975, 960, 715 cm^{-1}; MS, *m/z* (relative intensity) 188 (3), 186 (9), 149 (100), 85 (31), 71 (47), 57 (82), 41 (61).

Cyclization of α,α-Dichloro Ester Alkene 4e. Via the general procedure for cyclization, 201 mg (0.76 mmol) of dichloro ester **4e** was treated with 11.2 mg (0.012 mmol) of $RuCl_2(PPh_3)_3$ for 8 h to give 190 mg of a colorless oil, which GLC indicated contained a 62% yield of **34** and 12% of **35**. Purification of the compounds was done by preparative TLC (9:1 hexane/EtOAc), and the data for the pure isomers are listed below.

Fused α,γ-dichloro ester (34): bp 80–90 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (360 MHz, $CDCl_3$) δ 4.50 (1 H, ddd, *J* = 4.0, 6.0, 7.9 Hz), 4.25 (2 H, q, *J* = 7.1 Hz), 2.92 (1 H, dd, *J* = 6.0, 9.8 Hz), 2.46 (1 H, ddd, *J* = 8.4, 9.9, 13.9 Hz), 2.37 (1 H, m), 2.26–2.00 (2 H, m), 1.79 (1 H, m), 1.71–1.61 (5 H, m), 1.43 (1 H, m), 1.32 (3 H, t, *J* = 7.1 Hz); ^{13}C NMR (75 MHz, benzene-d_6) δ 170.6, 76.4, 62.2, 58.5, 55.9, 40.8, 36.1, 32.1, 30.2, 28.4, 20.0, 13.9; IR (film) 2960, 2925, 2855, 1735, 1455, 1435, 1360, 1265, 1205, 1090, 1030, 1010, 870, 855, 765 cm^{-1}; MS, *m/z* (relative intensity) 266 (0.34), 264 (0.53), 228 (19), 192 (41), 155 (68), 128 (44), 119 (100), 91 (74), 79 (54), 41 (37), 29 (59); exact mass calcd for $C_{12}H_{18}O_2Cl_2$ 264.0684, found 264.0674.

Fused α,γ-dichloro ester (35): mp 52–54 °C: bp 80–90 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (200 MHz, benzene-d_6) δ 4.10 (2 H, m), 3.51 (1 H, ddd, *J* = 4.6, 10.0, 11.3 Hz), 2.90 (1 H, ddd, *J* = 6.4, 11.6, 15.3 Hz), 2.78 (1 H, m), 2.49 (1 H, dd, *J* = 6.4, 10.0 Hz), 2.13 (1 H, m), 1.77 (1 H, m), 1.52–0.75 (7 H, m), 1.03 (3 H, t, *J* = 7.1 Hz); ^{13}C NMR (75 MHz, benzene-d_6) δ 169.9, 78.0, 62.4, 61.0, 58.3, 38.4, 37.8, 36.8, 26.0, 24.8, 20.5, 13.8; IR (film) 2980, 2935, 2865, 1730, 1470, 1445, 1370, 1265, 1215, 1065, 1025, 945, 865, 745 cm^{-1}; MS, *m/z* (relative intensity) 266 (1.2), 264 (2.0), 229 (14), 192 (32), 155 (34), 128 (53), 119 (100), 91 (64), 79 (53), 41 (33), 29 (50); exact mass calcd for $C_{12}H_{18}O_2Cl_2$ 264.0684, found 264.0668.

2aα-Chloro-3,4,4aα,5,6,7,7aα,7bα-(±)-octahydroindeno[7,1-*bc*]furan-2-one (36). Cyclization of dichloro acid **5e** (82 mg, 0.37 mmol) with $RuCl_2(PPh_3)_3$ (13.9 mg, 0.014 mmol) was carried out by using the general procedure. Heating the mixture for 18 h gave tricyclic lactone **36** as an oil, which was purified by preparative TLC to give 37 mg (50%) of a white solid: mp 62–62.5 °C (recrystallized from hexane); ^1H NMR (360 MHz, $CDCl_3$) δ 4.86 (1 H, ddd, *J* = 2.8, 6.5, 10.6 Hz), 2.75 (1 H, dd, *J* = 6.5, 10.6 Hz), 2.59 (1 H, dd, *J* = 5.5, 12.4 Hz), 2.49 (2 H, m), 2.25 (1 H, ddd, *J* = 6.3, 12.4, 13.6 Hz), 2.06 (1 H, m), 1.78–1.22 (7 H, m); ^{13}C NMR (50 MHz, benzene-d_6) δ 174.8, 74.9, 71.0, 47.2, 39.4, 35.6, 29.8, 27.6, 25.4, 13.2; IR (film) 2925, 2850, 1775, 1455, 1350, 1265, 1190, 1165, 1145, 975, 960, 905, 690 cm^{-1}.

Cyclization of α,α-Dichloro Ester Diene 4f. α,α-Dichloro ester diene **4f** (242 mg, 0.97 mmol) and $RuCl_2(PPh_3)_3$ (9.0 mg, 0.009 mmol) were dissolved in 4.0 mL of *tert*-butylbenzene. The mixture was deoxygenated with argon and heated at 150–155 °C for 2 h. Hexane (3 mL) and benzene (4 mL) were added to the reaction solution, producing a brown precipitate. The mixture was filtered through a 3-cm plug of Florisil, which was washed with 3 mL of benzene. The solvent was removed in vacuo to give 210 mg (87%) of a yellow oil, which GLC showed to contain **37** and **38** in 53:22 ratio, which were purified by preparative HPLC (hexane/EtOAc, 95:5). Data for these compounds are reported below.

Ethyl *trans*-1-chloro-2-((*E*)-3-chloroprop-1-enyl)cyclopentane-1-carboxylate (37): ^1H NMR (300 MHz, $CDCl_3$) δ 5.71 (1 H, dt, *J* = 6.4, 15.3 Hz), 5.60 (1 H, dd, *J* = 7.8, 15.3 Hz), 4.20 (2 H, q, *J* = 7.1 Hz), 3.98 (2 H, d, *J* = 6.4 Hz), 3.04 (1 H, dd, *J* = 7.8, 13.1 Hz), 2.56 (1 H, m), 2.31–1.63 (5 H, n), 1.29 (3 H, t, *J* = 7.1 Hz); IR (film) 2990, 2880,

1740, 1450, 1265, 1100, 1075, 1040, 975, 865 cm^{-1}; CIMS, m/z 253, 251 ($M^+ + 1$), 215.

Ethyl *cis*-1-chloro-2-((*E*)-3-chloroprop-1-enyl)cyclopentane-1-carboxylate (38): ^1H NMR (200 MHz, $CDCl_3$) δ 5.87 (1 H, dd, J = 7.3, 15.3 Hz), 5.67 (1 H, dt, J = 6.8, 15.3 Hz), 4.25 (2 H, q, J = 7.1 Hz), 3.08 (2 H, dd, J = 7.7, 17.4 Hz), 2.49–2.21 (2 H, m), 2.05–1.77 (5 H, m), 1.31 (3 H, t, J = 7.1 Hz); IR (film) 2990, 2880, 1735, 1450, 1375, 1265, 1185, 1160, 1105, 1035, 975, 870 cm^{-1}; CIMS, m/z 253, 251 ($M^+ + 1$), 215, 179.

Lactonization of a mixture of α,γ-dichloro esters **37** and **38** following the procedure described for the preparation of lactone **14** from **12** gave a mixture of epimeric γ-lactones **39**, which could be separated by HPLC (hexane/EtOAc, 8:2) along with recovered **37**. Data for the pure compounds are reported below.

α-Chloro γ-lactone 39 (less polar): ^1H NMR (200 MHz, $CDCl_3$) δ 5.82 (1 H, m), 5.44 (2 H, m), 5.23 (1 H, m), 2.96 (1 H, m), 2.62 (1 H, m), 2.24 (1 H, m), 1.98–1.53 (3 H, m), 1.30 (1 H, m); IR (film) 3510, 2975, 2880, 1785, 1480, 1445, 1380, 1205, 1150, 1005, 975, 905, 690 cm^{-1}; CIMS, m/z 189, 187 ($M^+ + 1$), 151.

α-Chloro γ-lactone 39 (more polar): ^1H NMR (200 MHz, $CDCl_3$) δ 5.96 (1 H, m), 5.36 (2 H, m), 4.54 (1 H, m), 2.88 (1 H, m), 2.54 (1 H, m), 2.32–1.65 (4 H, m), 1.31 (1 H, m); IR (film) 3510, 2975, 2880, 1785, 1480, 1445, 1380, 1205, 1150, 1005, 975, 905, 690 cm^{-1}; CIMS, m/z 189, 187 ($M^+ + 1$), 151.

Ethyl 2-(Chloromethyl)cyclopent-1-ene-1-carboxylate (44). By the application of the procedure used for the cyclization of **4f**, 127 mg (0.57 mmol) of acetylenic α,α-dichloro ester **4g** was heated at 150–155 °C in 4 mL of cumene for 4 h with 6.2 mg (0.007 mmol) of $RuCl_2(PPh_3)_3$ to give 79 mg (74%) of a colorless oil after distillation. GLC analysis indicated this crude material had α,β-unsaturated ester **44** as the major component (94%): bp 45–50 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (200 MHz, benzene-d_6) δ 4.60 (2 H, d, J = <1 Hz), 3.92 (2 H, q, J = 7.1 Hz), 2.48 (2 H, m), 2.32 (2 H, m), 1.42 (2 H, m), 0.92 (3 H, t, J = 7.1 Hz); ^{13}C NMR (50 MHz, benzene-d_6) δ 164.6, 151.8, 131.7, 60.0, 40.2, 36.2, 34.1, 21.1, 14.1; IR (film) 2975, 2940, 2845, 1705, 1635, 1430, 1365, 1335, 1295, 1260, 1190, 1105, 1035, 765, 705 cm^{-1}; MS, m/z (relative intensity) 190 (19), 188 (57), 160 (50), 143 (47), 49 (22), 29 (43); exact mass calcd for $C_9H_{13}O_2Cl$ 188.604, found 188.0596.

Ethyl 1-Chloro-2-(1-chloroethyl)cyclopent-1-ene-1-carboxylate (45). Acetylenic dichloro ester **4h** (145 mg, 0.61 mmol) was heated in refluxing toluene with 23 mg (0.024 mmol) of $RuCl_2(PPh_3)_3$ for 12 h to give 104 mg of **45** as a yellow oil, which was pure (99%) by GLC (83% yield). Attempted purification of the crude material by preparative TLC resulted in extensive decomposition of the product: bp 35–45 °C (<0.1 Torr, bulb-to-bulb); ^1H NMR (200 MHz, benzene-d_6) δ 6.24 (1 H, q, J = 6.8 Hz), 3.92 (2 H, q, J = 7.1 Hz), 2.73–2.08 (4 H, m), 1.44 (2 H, m), 1.38 (3 H, d, J = 6.8 Hz), 0.92 (3 H, t, J = 7.1 Hz); ^{13}C NMR (50 MHz, benzene-d_6) δ 164.7, 156.7, 129.4, 60.0, 52.8, 34.0, 32.7, 23.6, 21.3, 14.1; IR (film) 2975, 2920, 2895, 2850, 1705, 1625, 1440, 1365, 1325, 1295, 1220, 1180, 1155, 1075, 1025, 765 cm^{-1}.

Cyclization of Olefinic α,α-Dichloro-β-keto Ester 7a. Cyclization of β-keto dichloro ester **7a** (200 mg, 0.89 mmol), with 2.8 mg of CuCl (0.029 mmol) and 4.1 mg of PPh_3 (0.016 mmol) was performed by using the procedure for cyclization of **4f**. Bulb-to-bulb distillation [bp 50–60 °C (30 Torr)] of the brown residue gave 159 mg of a light yellow oil, which by GLC was a 1.6:2.5:1.4:1 mixture of **46**, **47**, and the epimeric endo isomers **48**. The compounds were separated by HPLC (hexane/EtOAc, 9:1), and the data for each are reported below.

Methyl *trans*-1-chloro-2-(chloromethyl)-3-oxocyclopentane-1-carboxylate (46): ^1H NMR (200 MHz, $CDCl_3$) δ 3.91 (1 H, dd, J = 4.4, 11.2 Hz), 3.81 (3 H, s), 3.51 (1 H, dd, J = 9.0, 11.2 Hz), 2.85–2.39 (4 H, m), 2.04 (1 H, m); IR (film) 2960, 2900, 1760, 1725, 1440, 1405, 1245, 1160, 1095, 1005, 935, 900, 790 cm^{-1}; MS, m/z (relative intensity) 228 (1.4), 226 (5.6), 224 (9.1), 188 (100), 169 (40), 160 (88), 133 (65), 59 (74), 55 (59), 39 (68); exact mass calcd for $C_8H_{10}O_3Cl_2$ 224.0007, found 223.9993.

Methyl *cis*-1-chloro-2-(chloromethyl)-3-oxocyclopentane-1-carboxylate (47): ^1H NMR (200 MHz, $CDCl_3$) δ 3.85 (3 H, s), 3.75 (1 H, dd, J = 8.8, 11.1 Hz), 3.62 (1 H, dd, J = 5.9, 11.1 Hz), 3.32 (1 H, m), 2.79–2.19 (3 H, m), 1.79 (1 H, m); IR (film) 2970, 2900, 1760, 1740, 1440, 1410, 1245, 1195, 1160, 1095, 1055, 1020, 860, 810, 770, 750 cm^{-1}; MS, m/z (relative intensity) 228 (1.1), 226 (7.2), 224 (11.2), 188 (64), 169 (22), 160 (51), 133 (39), 59 (47), 55 (52), 49 (100), 39 (68); exact mass calcd for $C_8H_{10}O_3Cl_2$ 224.0007, found 224.0006.

α,γ-Dichloro-β-keto ester 48 (major): ^1H NMR (200 MHz, $CDCl_3$) δ 4.57 (1 H, m), 3.87 (3 H, s), 3.08 (2 H, m), 2.79–2.41 (3 H, m), 2.17 (1 H, m); IR (film) 2970, 2940, 1760, 1735, 1440, 1330, 1265, 1075, 1040, 890, 790, 765, 730 cm^{-1}; MS, m/z (relative intensity) 228 (3.6), 226 (20), 224 (32), 189 (4.9), 161 (78), 59 (67), 55 (100), 42 (60), 28 (40); exact mass calcd for $C_8H_{10}O_3Cl_2$ 224.0007, found 224.0003.

α,γ-Dichloro-β-keto ester 48 (minor): ^1H NMR (200 MHz, $CDCl_3$) δ 4.27 (1 H, m), 3.86 (3 H, s), 3.35 (1 H, ddd, J = 3.1, 4.0, 13.4 Hz), 2.84–2.31 (4 H, m), 2.06 (1 H, m); IR (film) 2965, 2940, 1765, 1735, 1440, 1265, 1235, 1140, 1100, 980, 895, 860, 825 cm^{-1}; MS, m/z (relative intensity) 228 (2.4), 226 (14), 224 (21), 188 (25), 161 (63), 59 (77), 55 (92), 39 (100), 28 (62); exact mass calcd for $C_8H_{10}O_3Cl_2$ 224.0007, found 224.0004.

Cyclization of Olefinic α,α-Dichloro-β-keto Ester 7b. Via the procedure described for the cyclization of **7a**, 205 mg (0.92 mmol) of β-keto ester **7b** was heated at 150–155 °C in *tert*-butylbenzene with 4.7 mg (0.081 mmol) of CuCl and 4.7 mg (0.018 mmol) of PPh_3 for 12 h to give 159 mg (78%) of a yellow oil, which was found by GLC to be a mixture of **49** (10%) and the two epimers of **50** (53%/8%), which were separated by HPLC (hexane/EtOAc, 9:1). Data for the pure compounds are given below.

Fused α,γ-dichloro-β-keto ester (49): mp 52.5–56 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 4.51 (1 H, m), 3.84 (3 H, s), 3.39 (1 H, m), 2.72 (2 H, m), 2.40 (2 H, m), 1.98–1.48 (7 H, m); IR (film) 2950, 2875, 1770, 1735, 1440, 1410, 1260, 1040, 1010, 905, 845, 775 cm^{-1}; MS, m/z (relative intensity) 268 (2.7), 266 (16), 264 (25), 238 (32), 236 (49), 201 (48), 193 (69), 161 (90), 105 (97), 74 (100), 49 (51), 41 (96); exact mass calcd for $C_{12}H_{16}O_3Cl_2$ 264.0320, found 264.0326.

Fused α,γ-dichloro-β-keto ester 50 (major): bp 110–115 °C (bulb-to-bulb); ^1H NMR (200 MHz, $CDCl_3$) δ 4.07 (1 H, dt, J = 4.5, 10.7 Hz), 3.85 (3 H, s), 3.05 (1 H, m), 2.82 (1 H, dd, J = 6.1, 10.4 Hz), 2.48–2.18 (3 H, m), 1.85–1.50 (5 H, m); IR (film) 2960, 2875, 1760, 1730, 1630, 1435, 1285, 1175, 1150, 1075, 995, 840, 760 cm^{-1}; MS, m/z (relative intensity) 268 (2.5), 266 (15), 264 (24), 236 (37), 193 (62), 161 (100), 105 (81), 91 (70), 59 (65), 41 (85); exact mass calcd for $C_{12}H_{16}O_3Cl_2$ 264.0320, found 264.0305.

Fused α,γ-dichloro-β-keto ester 50 (minor): mp 36–38.5 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 4.42 (1 H, m), 3.84 (3 H, s), 3.45 (1 H, m), 2.65–2.30 (4 H, m), 2.01–1.45 (5 H, m); IR (film) 2955, 2875, 1765, 1730, 1445, 1405, 1250, 1050, 895, 870, 810, 750 cm^{-1}; MS, m/z (relative intensity) 268 (1.2), 266 (7.4), 264 (11), 238 (65), 236 (100), 195 (30), 161 (80), 105 (61), 59 (50), 41 (68); exact mass calcd for $C_{12}H_{16}O_3Cl_2$ 264.0320, found 264.0324.

Copper-Promoted Cyclization of Olefinic α,α-Dichloro Nitrile 9b. Cyclization of dichloro nitrile **9b** (169 mg, 0.88 mmol) with CuCl (1.0 mg, 0.01 mmol) and PPh_3 (2.0 mg, 0.01 mmol) was carried out by applying the general procedure for the cyclization of **4a** (21 h). Purification of the yellow oil on two 20 × 20 cm preparative TLC plates (hexane/EtOAc, 19:1) gave 136 mg (91%) of a colorless oil, which by GLC was found to be a mixture of isomers of **51** in a 1.0:1.2 ratio. The isomers could be purified by preparative TLC by eluting twice with 19:1 hexane/EtOAc. Data for the purified compounds are reported below.

α,γ-Dichloro nitrile 51 (major isomer): ^1H NMR (200 MHz, $CDCl_3$) δ 4.15 (1 H, dd, J = 3.0, 11 Hz), 3.54–3.39 (2 H, m), 2.59–2.56 (1 H, m), 2.54–2.50 (1 H, m), 2.09–1.84 (2 H, m), 1.41–1.22 (4 H, m); IR (film) 2960, 2870, 2250, 1450, 900, 880, 860, 780, 755 cm^{-1}; MS, m/z (relative intensity) 195 (2), 193 (11), 191 (18), 156 (47), 120 (61), 104 (43), 81 (37), 68 (96), 55 (100), 41 (89), 27 (48); exact mass calcd for $C_8H_{11}Cl_2N$ 191.0269, found 191.0268.

α,γ-Dichloro nitrile 51 (minor isomer): ^1H NMR (200 MHz, $CDCl_3$) δ 3.94 (1 H, dd, J = 3.1, 11.1 Hz), 3.54–3.37 (2 H, m), 2.37–2.02 (2 H, m), 1.87–1.66 (2 H, m), 1.52–1.18 (4 H, m); IR (film) 2960, 2870, 2250, 1450, 975, 965, 905, 870, 850, 800, 760 cm^{-1}; MS, m/z (relative intensity) 195 (1), 193 (5), 191 (8), 156 (45), 120 (63), 81 (31), 68 (99), 55 (100), 41 (85), 27 (52).

Cyclization of α,α-Dichloro Nitrile 9c. Dichloro nitrile **9c** (197 mg, 0.99 mmol), CuCl (2.6 mg, 0.03 mmol), and PPh_3 (3.6 mg, 0.01 mmol) were cyclized by using the procedure described above for **9b** (8 h of heating) and gave 189 mg of a colorless oil, which by GLC was calculated to contain a 61% yield of **53** and a 33% yield of **54**. The isomers could be purified by preparative TLC, eluting twice with 19:1 hexane/EtOAc. Data for the purified compounds are reported below.

***endo*,*exo*-1,3-Dichlorobicyclo[2.2.1]heptane-*exo*-1-nitrile (53)**: mp 43–44 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 4.61–4.55 (1 H, m), 3.00 (1 H, br s), 2.66–2.52 (2 H, m), 2.23–1.69 (5 H, m); IR (film) 2990, 2950, 2900, 2875, 2250, 1470, 1450, 930, 860, 790 cm^{-1}; MS, m/z (relative intensity) 155 (15), 153 (43), 118 (100), 102 (38), 91 (23), 67 (98), 49 (53); exact mass calcd for $C_8H_9Cl_2N$ 189.0112, found 189.0100.

***exo*,*exo*-1,3-Dichlorobicyclo[2.2.1]heptane-*endo*-1-nitrile (54)**: colorless oil; ^1H NMR (200 MHz, $CDCl_3$) δ 4.35–4.29 (1 H, m), 2.91 (1 H, s), 2.57 (2 H, d, J = 3.0 Hz), 2.38–1.69 (5 H, m); IR (film) 2990, 2950, 2900, 2875, 2250, 1470, 1450, 930, 860, 790 cm^{-1}; MS, m/z (relative intensity) 155 (13), 153 (38), 118 (89), 91 (26), 67 (100), 49 (96), 28 (83); exact mass calcd for $C_8H_9Cl_2N$ 189.0112, found 189.0110.

Cyclization of Olefinic α,α-Dichloro Nitrile 9d. Via the procedure described above, 148 mg (0.72 mmol) of **9d** was treated with 2.1 mg (0.02

mmol) of CuCl and PPh_3 (5.6 mg, 0.02 mmol) for 9.5 h to give 133 mg of a mixture of two compounds (34% yield of **55**, 40% yield of **56** by GLC), which could be separated by preparative TLC by eluting once with 19:1 hexane/EtOAc. Data for the pure compounds are reported below.

***endo*,*exo*-1,3-Dichlorobicyclo[3.2.1]octane-*exo*-1-nitrile (55)**: ^1H NMR (200 MHz, $CDCl_3$) δ 4.54-4.52 (1 H, m), 2.93 (1 H, dd, J = 7.4, 15.1 Hz), 2.85-2.83 (1 H, m), 2.46-2.10 (4 H, m), 1.99-1.85 (4 H, m); IR (film) 2950, 2870, 2250, 1460, 855, 830, 800, 780, 760, 675, 620 cm^{-1}; MS, m/z (relative intensity) 169 (5), 167 (13), 132 (39), 116 (24), 80 (100), 49 (45), 39 (21), 28 (26); exact mass calcd for $C_9H_{11}Cl_2N$ 203.0269, found 203.0278.

***exo*,*exo*-1,3-Dichlorobicyclo[4.2.1]octane-*endo*-1-nitrile (56)**: ^1H NMR (200 MHz, $CDCl_3$) δ 4.55-4.53 (1 H, m), 2.85-2.81 (1 H, m), 2.71-2.51 (3 H, m), 2.34 (1 H, d, J = 12.6 Hz), 2.26-1.81 (5 H, m); IR (film) 2950, 2860, 2250, 1460, 840, 810, 780, 750, 675 cm^{-1}; MS, m/z (relative intensity) 169 (8), 167 (17), 132 (40), 116 (24), 80 (87), 49 (100), 39 (18); exact mass calcd for $C_9H_{11}Cl_2N$ 203.0269, found 203.0273.

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Stereochemical Controls on Exciplex Reactions. Excited State Proton Transfer

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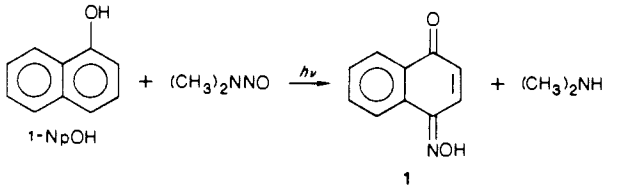
Abstract: By the use of the interaction of excited-state 1-naphthol (1-NpOH) and *N*-nitrosodimethylamine (NND) as the model, it is shown that excited state proton transfer in organic solvents is a diffusion-controlled process and requires high degrees of geometric arrangements in comparison to energy and charge (electron) transfer processes. During the interaction two identifiable singlet exciplexes can be implicated; one is derived from the direct excitation of the ground-state complex of 1-NpOH and NND and does not proceed to self-nitrosation, while the other is formed from a dynamic collision of *1-NpOH and NND and leads to self-nitrosation to yield 1,4-naphthoquinone monooxime. Each exciplex does not interconvert to the other owing to rapid proton transfer or energy-transfer processes within exciplexes. A possible structure of the ground-state complex was inferred from the NMR chemical shifts displayed by 1-NpOH aromatic protons in the presence of increasing NND concentrations.

We have established that the photoexcitation of polycyclic phenols (ArOH) in the presence of *N*-nitrosodimethylamine (NND) induces nitrosation of the phenols and that the excited state proton transfer (ESPT) from singlet excited state phenols (*ArOH) to NND is the indispensable step to cause the observed photoreaction.[3] For example, photolysis of 1-naphthol (1-NpOH) in the presence of NND led to the formation of 1,4-naphthoquinone monooxime (**1**). The mechanistic studies of this self-photonitrosation failed to detect a new emission peak of $*NpO^-$ arising from ESPT, but the presence of an exciplex was assumed. Further investigations show that a ground-state complex between 1-NpOH (and other phenols) and NND is formed in solution and that the mechanism of the interaction of excited state *1-NpOH and NND is more complicated than what had been assumed. In this paper we establish the presence of two exciplexes that are not interconvertible during the lifetime of *1-NpOH.



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Results

The UV absorption spectra of 1-NpOH in the presence of NND clearly showed an additional absorption in the 360-450-nm region where both substrates showed no appreciable absorption. The new absorption, assigned to that of a ground-state complex of 1-NpOH-NND (X_S), was partly superimposed with NND absorption in the 360-400-nm region[4] and was unambiguously demonstrated by differential absorption spectra, in dioxane (see Figure 1 in ref 3b), which were taken by using the individual solutions of the substrates in dioxane as the reference. On the assumption of a 1:1 complex formation between 1-NpOH and NND, the association constant, K, was calculated according[5] to eq 1 at various wavelengths (Table I); in this equation, OD°, OD, and OD′ are the absorbances at a certain wavelength of three solutions containing concentrations of zero, C_A, and C_A' of the component A at a fixed concentration of the component B.

$$K = \frac{C_A(OD° - OD') + C_A'(OD - OD°)}{C_A C_A'(OD' - OD)} \quad (1)$$

Table I. Association Constants (K) of the Ground-State Complex between 1-NpOH and NND in Dioxane[a] at 20 °C

monitoring wavelength, nm	optical density: [NND], M			K, M^{-1}	
	0.030	0.050	0.150	*b*	*c*
398	0.0058	0.0095	0.0180	5.5	8.2
400	0.0053	0.0084	0.0160	6.5	8.0
402	0.0050	0.0080	0.0150	6.7	8.5
			average	6.2	8.3

[a] [1-NpOH] = 3×10^{-4} M. [b] Calculated from the data of [NND] of 0.030 M and 0.150 M. [c] Calculated from the data of [NND] of 0.050 M and 0.150 M.

The formation of a ground-state complex, X_S, between 1-NpOH and NND was further demonstrated by NMR spectroscopy, which confirmed the stoicheometry[6-9] of 1:1. The presence of collisional

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