reacted with an aniline. Other methods include the reaction of an acid anhydride with an aniline under pressure[13] and the reaction of a carboxylic acid with an aniline under dehydrating conditions.[14] In all of these methods, the formation of 4-nitroanilides is one of the most difficult ones because of the low basicity of 4-nitroaniline or the interference of the nitro group with the aminomagnesium halide reagent,[11] respectively. The yields reported here for the 4-nitroanilides range from fair to good. The anilides were identified by their elemental analysis, by UV, IR, NMR spectra,[1a] and, when available, by comparison with authentic materials. The reported yields are based on one run only. In attempts to optimize the yield of this autoxidation reaction by using 18-crown-6 ether or hexamethylphosphoric triamide (HMPT),[15] no significant improvement was obtained.

Experimental Section

All melting points are uncorrected. The elemental analyses were performed by Integral Microanalytical Laboratories.

The general procedure for the preparation of anilides is as follows. In a Parr pressure bottle, the phosphonate (0.005 mol) was dissolved in 10 mL/g of Me_2SO. To this solution, potassium *tert*-butoxide (0.0055 mol) was added. Quickly, the bottle was stoppered and placed on a Parr hydrogenation low-pressure apparatus and filled with oxygen until a pressure of 50 psi was reached. After 12 h, the now dark solution was diluted with 250 mL of H_2O and extracted twice with ethyl ether. The combined ether extracts were successively washed with water and brine and then dried over anhydrous sodium sulfate. Evaporation of the ether under vacuum left a clean solid residue which was recrystallized from a suitable solvent.

Acknowledgment. This investigation was partially supported by Grant CA-16666, awarded by the National Cancer Institute, DHEW.

Registry No. 1, 73230-90-7; 2, 73230-91-8; 3, 73230-92-9; 4, 73230-93-0; 5, 73230-94-1; 6, 73230-95-2; 7, 73246-60-3; 8, 39880-88-1; 9, 73230-96-3; 10, 73230-97-4; 11, 15341-97-6; 12, 33667-88-8; 13, 73230-98-5; 14, 73261-73-1.

(12) V. Gold, J. Hilton, and E. G. Jefferson, *J. Chem. Soc.*, 2756 (1954), and references therein.
(13) L. F. Golovyashkina, *Uzb. Khim. Zh.*, 11, 24 (1967); *Chem. Abstr.*, 64136 (1967).
(14) H. R. Snyder and C. T. Elston, *J. Am. Chem. Soc.*, **76**, 3039 (1954). Using *p*-nitroaniline in their method, these authors obtained a yield of 0% of the desired *p*-nitroanilide.
(15) H. J. Bestmann and W. Stransky, *Synthesis*, 798 (1974).

Studies on Ketene and Its Derivatives. 98.[1] 1,1-Dichloro-5-oxo-4-oxaspiro[2.3]hexane. Synthesis and Reactions

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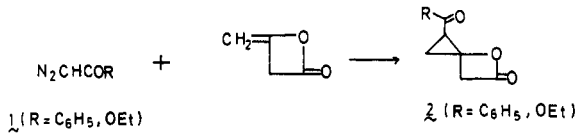
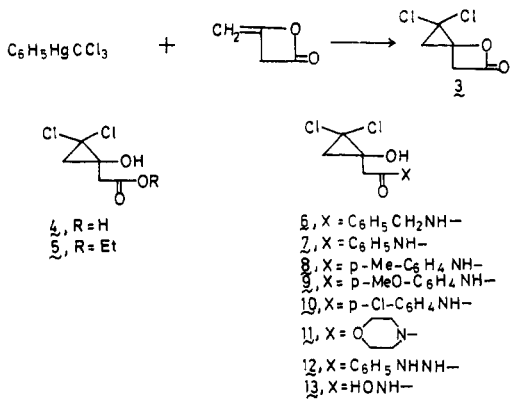
Previously, we reported that α-diazo ketones and esters, such as diazoacetophenone (1, R = Ph) and ethyl diazoacetate (1, R = OEt), react with diketone to give the spiro compounds 1-benzoyl- (and 1-ethoxycarbonyl-) 5-oxo-4-oxaspiro[2.3]hexane (2, R = Ph and OEt)[2,3] (see Scheme I). The reaction involves [1 + 2] cycloaddition of a carbene generated from the diazo compound to the exo methylene of diketene. In the present paper, we describe that the reaction of diketene with phenyl(trichloromethyl)mercury, which can be regarded as a carbene precursor, proceeds in a similar fashion to give a spiro compound. Furthermore, we have investigated some reactions of the product to give cyclopropaneacetic acid derivatives in which the cyclopropane ring remains intact. Since the reactions of the cyclopropanespirolactones of type 2 under the same conditions gave ring-opened products, it is of interest that dichlorocyclopropanespirolactone does not suffer opening of the three-membered ring. These results are another subject of the present paper.

Scheme I



Scheme II



When a solution of phenyl(trichloromethyl)mercury and diketene in dry benzene was refluxed, the spiro compound 1,1-dichloro-5-oxo-4-oxaspiro[2.3]hexane (3) was obtained in 25% yield (see Scheme II). When dry toluene was used as a solvent instead of benzene, the reaction proceeded more smoothly to give 3 in 72% yield.

Structure assignment of the products was made on the basis of elemental analyses, spectral data, and chemical behavior. Specifically, the IR spectrum of 3 showed the presence of the β-lactone carbonyl at 1865 cm^{-1}, and the NMR spectrum indicated two AB quartet signals assignable to the methylene groups of the cyclopropane and β-lactone rings at δ 1.84–2.27 and 3.47–4.10, respectively.

Hydrolysis of spiro product 3 with 10% hydrochloric acid afforded 2,2-dichloro-1-hydroxycyclopropaneacetic acid (4) in 60% yield. In its IR spectrum the β-lactone carbonyl absorption had disappeared and hydroxyl and carboxylic acid absorptions were observed at 3600–2400, 3530, and 1715 cm^{-1}. The NMR spectrum showed two singlet signals due to the methylene groups of the cyclopropane and acetic acid moieties at δ 1.69 and 2.97, respectively.

Treatment of 3 with dry hydrogen chloride in absolute ethanol gave ethyl 2,2-dichloro-1-hydroxycyclopropaneacetate (5) as a colorless oil in 81% yield. As detailed in the Experimental Section, the IR and NMR spectra were consistent with ester structure 5.

Treatment of 3 with an alkali such as sodium bicarbonate in water or sodium ethoxide in ethanol resulted

(1) No. 97: T. Kato, T. Chiba, and S. Tsuchiya, *Chem. Pharm. Bull.*, **28**, 327 (1980).
(2) T. Kato, N. Katagiri, and R. Sato, *J. Chem. Soc., Perkin Trans. 1*, 525 (1979).
(3) T. Kato and N. Katagiri, *Chem. Pharm. Bull.*, **21**, 729 (1973).

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Table I. Reaction of 3 with Amines

3, mmol	amine (mmol)	product no.	product X	mp, °C	conditions: solvent	conditions: temp, °C	conditions: time, h	yield, %
3	benzylamine (3)	6	$C_6H_5CH_2NH$	94	CCl_4	−15	2	60
3	aniline (3)	7	C_6H_5NH	130–131[a]	$CHCl_3$	20	9	51
3	*p*-toluidine (3)	8	*p*-MeC_6H_4NH	127.5[a]	Et_2O	20	9	59
3	*p*-anisidine (3)	9	*p*-$MeOC_6H_4NH$	122[a]	Et_2O	20	9	56
3	*p*-chloroaniline (3)	10	*p*-ClC_6H_4NH	111	$CHCl_3$	20	9	80
2	morpholine (2)	11		111	$CHCl_3$	20	9	79
3	phenylhydrazine (3)	12	C_6H_5NHNH	136[a]	EtOH	20	24	69
3	hydroxylamine·HCl (3.6); AcONa (3.6)	13	HONH	126[a]	EtOH	0	60	41

[a] Decomposition.

Table II. Spectroscopic Data and Analyses for 6–13

prod no.	IR, cm^{-1} ($CHCl_3$)	NMR, δ (Me_2SO-d_6)	formula	analysis, % calcd (found): C	H	N
6	3340[a] 3300 1650	1.56–1.89 (AB q, J = 8.4 Hz, 2 H), 2.50–2.98 (AB q, J = 14.5 Hz, 2 H), 4.21–4.48 (m, 2 H), 7.31 (s, 5 H), 8.48 (br, 1 H)	$C_{12}H_{13}Cl_2NO_2$	52.57 (52.50)	4.75 (4.77)	5.11 (5.10)
7	3340 3330 1675	1.58–1.98 (AB q, J = 8.4 Hz, 2 H), 2.57–3.16 (AB q, J = 16.8 Hz, 2 H), 7.03–7.74 (m, 5 H), 9.97 (br, 1 H)	$C_{11}H_{11}Cl_2NO_2$	50.79 (50.88)	4.23 (4.39)	5.39 (5.43)
8	3420 3320 1675	1.60–2.00 (AB q, J = 9.0 Hz, 2 H), 2.30 (s, 3 H), 2.60–3.18 (AB q, J = 15.0 Hz, 2 H), 7.15–7.32 (m, 2 H), 7.55–7.25 (m, 2 H), 10.01 (br, 1 H)	$C_{12}H_{13}Cl_2NO_2$	52.57 (52.85)	4.75 (4.73)	5.11 (5.08)
9	3440 3350 1675	1.60–1.99 (AB q, J = 9.0 Hz, 2 H), 2.58–3.17 (AB q, J = 15.0 Hz, 2 H), 3.78 (s, 3 H), 6.88–7.13 (m, 2 H), 7.51–7.82 (m, 2 H), 10.01 (br, 1 H)	$C_{12}H_{13}Cl_2NO_3$	49.67 (49.67)	4.48 (4.47)	4.83 (4.72)
10	3420 3240 1665	1.62–2.00 (AB q, J = 9.0 Hz, 2 H), 2.60–3.20 (AB q, J = 14.8 Hz, 2 H), 7.29–7.80 (m, 4 H), 11.13 (br, 1 H)	$C_{11}H_{10}Cl_3NO_2$	44.84 (45.00)	3.40 (3.16)	4.76 (4.75)
11	3480 1640	1.37–1.79 (AB q, J = 9.0 Hz, 2 H), 2.58–3.22 (AB q, J = 16.0 Hz, 2 H), 3.17–3.80 (m, 8 H), 5.53 (br s, 1 H)[b]	$C_9H_{13}Cl_2NO_3$	42.54 (42.64)	5.12 (5.20)	5.51 (5.59)
12	3390[a] 3250 1670	1.57–1.95 (AB q, J = 8.6 Hz, 2 H), 2.45–3.05 (AB q, J = 14.8 Hz, 2 H), 6.58–7.45 (m, 5 H), 9.70 (s, 1 H)	$C_{11}H_{12}Cl_2N_2O_2$	48.02 (47.94)	4.37 (4.65)	10.19 (10.11)
13	3410[a] 3280 1640	1.51–1.87 (AB q, J = 9.0 Hz, 2 H), 2.22–2.80 (AB q, J = 14.8 Hz, 2 H)	$C_5H_7Cl_2NO_3$	30.02 (30.00)	3.50 (3.41)	7.00 (6.96)

[a] Measured in KBr disk. [b] Measured in $CDCl_3$.

in the formation of a resinous product.

Reactions of **3** with amines gave cyclopropaneacetamide derivatives (see Table I). Benzylamine reacted with **3** to give *N*-benzyl-2,2-dichloro-1-hydroxycyclopropaneacetamide (**6**) in 60% yield. Similarly, aniline, *p*-toluidine, *p*-anisidine, and *p*-chloroaniline were allowed to react with **3** to give the corresponding cyclopropaneacetanilide derivatives **7**, **8**, **9**, and **10** in 50–80% yield. The similar reaction of compound **3** with morpholine gave cyclopropaneacetamide (**11**) in 79% yield.

Reaction of **3** with carbonyl reagents such as phenylhydrazine and hydroxylamine afforded the cyclopropane derivatives *N*-anilino-2,2-dichloro-1-hydroxycyclopropaneacetamide (**12**) and *N*-hydroxy-2,2-dichloro-1-hydroxycyclopropaneacetamide (**13**) in 69 and 41% yields, respectively. Structure assignments of these products were made on the basis of elemental analyses and spectroscopic data, detailed in Table II.

Experimental Section

IR spectra were taken with a JASCO IR-S spectrophotometer. NMR spectra were measured with a Hitachi R-20 instrument with tetramethylsilane as an internal standard. Melting and boiling points are uncorrected.

1,1-Dichloro-5-oxo-4-oxaspiro[2.3]hexane (3). (i) A solution of phenyl(trichloromethyl)mercury (7.0 g, 0.018 mol) and diketene (5.9 g, 0.07 mol) in dry toluene (30 mL) was heated under reflux for 4 h with stirring. The reaction mixture was cooled, and the precipitate was collected by suction filtration to give a phenylmercuric chloride: mp 248–250 °C (lit.[4] mp 256–258 °C), 10.9 g (99%). The filtrate was condensed under reduced pressure, and the residue was extracted with ether. The ether solution was condensed, and the brown oily residue was distilled under reduced pressure to give **3** as a colorless oil, 4.2 g (75%): bp 68–70 °C (3 mm); IR ($CHCl_3$) 3035, 1890 (sh), 1865, 1850 (sh) cm^{-1}; NMR ($CDCl_3$) δ 1.84–2.27 (AB q, 2 H, J = 10.2 Hz, cyclopropane ring protons), 3.47–4.10 (AB q, 2 H, J = 16.8 Hz, β-lactone ring protons); mass spectrum, m/e 167 (M^+).

Anal. Calcd for $C_5H_4Cl_2O_2$: C, 35.96; H, 2.42; Cl, 42.51. Found: C, 36.06; H, 2.26; Cl, 42.62.

(ii) In similar fashion, a mixture of phenyl(trichloromethyl)mercury (7.0 g) and diketene (3.0 g, 0.036 mol) in dry benzene (30 mL) was refluxed for 40 h to give **3** in 25% yield (0.75 g).

(4) D. Seyferth and J. M. Burlitch, *J. Organomet. Chem.*, 4, 127 (1965).

2,2-Dichloro-1-hydroxycyclopropaneacetic Acid (4). A suspension of **3** (3.1 g) in 10% hydrochloric acid (12 mL) was heated at 50–60 °C on a steam bath with stirring. The reaction mixture was condensed under reduced pressure to give a viscous residue which was allowed to stand at room temperature to form a crystalline substance. Recrystallization from petroleum ether (bp 60–70 °C) afforded **4** as needles, 2.1 g (60%): mp 99–100 °C; IR ($CHCl_3$) 3600–2400, 3530, 1715 cm^{-1}; NMR (acetone-d_6) δ 1.69 (s, 2 H, cyclopropane ring protons), 2.97 (s, 2 H CH_2CO_2H), 5.55 (br s, 1 H, D_2O exchangeable, OH), 7.30 (br s, 1 H, D_2O exchangeable, COOH).

Anal. Calcd for $C_5H_6Cl_2O_3$: C, 32.45; H, 3.24; Cl, 38.35. Found: C, 32.47; H, 3.15; Cl, 38.29.

Ethyl 2,2-Dichloro-1-hydroxycyclopropaneacetate (5). A solution of **3** (4.0 g, 0.024 mol) in absolute ethanol (10.0 g, 0.22 mol) was saturated with dry hydrogen chloride under ice–salt cooling. The reaction mixture was heated at 50–60 °C on a steam bath for 7 h. Evaporation of ethanol left an oily residue which was distilled under reduced pressure to give **5** as a colorless oil, 4.2 g (81%): bp 82–83 °C (4 mm); IR ($CHCl_3$) 3500, 2970, 1715 cm^{-1}; NMR ($CDCl_3$) δ 1.31 (t, 3 H, J = 7.2 Hz, OCH_2CH_3), 1.41–1.80 (AB q, 2 H, J = 9.6 Hz, cyclopropane ring protons), 2.58–3.34 (AB q, 2 H, J = 18.0 Hz, CH_2CO_2Et), 4.25 (br s, 1 H, D_2O exchangeable, OH), 4.31 (q, 2 H, J = 7.2 Hz, OCH_2CH_3).

Anal. Calcd for $C_7H_{10}Cl_2O_3$: C, 39.46; H, 4.70; Cl, 33.30. Found: C, 39.74; H, 4.73; Cl, 32.93.

General Procedure for the Synthesis of 2,2-Dichloro-1-hydroxycyclopropaneacetamide Derivatives 6–13. A solution of **3** and the chosen amine in the organic solvent shown in Table I was stirred. Precipitates were collected by suction filtration. Purification by recrystallization gave compounds **6–13**. Reaction conditions, results, and physical data are summarized in Tables I and II.

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Registry No. 3, 73090-43-4; **4**, 73090-44-5; **5**, 73090-45-6; **6**, 73090-46-7; **7**, 73090-47-8; **8**, 73090-48-9; **9**, 73090-49-0; **10**, 73090-50-3; **11**, 73104-81-1; **12**, 73090-51-4; **13**, 73090-52-5; benzylamine, 100-46-9; aniline, 62-53-3; *p*-toluidine, 106-49-0; *p*-anisidine, 104-94-9; *p*-chloroaniline, 106-47-8; morpholine, 110-91-8; phenylhydrazine, 100-63-0; hydroxylamine hydrochloride, 5470-11-1; phenyl(trichloromethyl)mercury, 3294-57-3; diketene, 674-82-8; ethanol, 64-17-5.

Syntheses of α-Chloro Ketones by Reaction of Silyl Enol Ethers with $CuCl_2$ and $FeCl_3$

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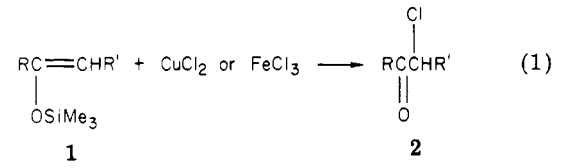
We have already reported a series of reactions of silyl ethers of enols and cyclopropanols with metal salts,[1] in which metal enolates and metal cyclopropoxides may be assumed as key intermediates. Now we wish to report the reactions of silyl enol ethers with cupric chloride and ferric chloride to produce α-chloro ketones according to eq 1. The reaction provides a simple and convenient synthetic method for the preparation of α-chloro ketones under mild conditions. For the chlorination of silyl enol ethers we have obtained some results which are taken to suggest a reaction



1 2 (1)

mechanism involving a vinyloxy radical generated from the collapse of the copper(II) or iron(III) enolate which was formed initially.

Reaction of Silyl Enol Ethers with Anhydrous $CuCl_2$. When silyl enol ethers (**1**) were treated with a 2 or 3 molar excess of cupric chloride in dimethylformamide (DMF), α-chloro ketones (**2**) were produced in moderate yields together with the starting ketones.

The selection of specific solvents was very important for all of the reactions of silyl ethers of enols and cyclopropanols with metal salts. The use of DMF in the present reaction played a decisive role. No reaction occurred in other common organic solvents. Some results are summarized in Table I. Interesting features of the chlorination of silyl enol ethers with cupric chloride are as follows: (i) α-chlorination of unsymmetrical ketones can be regiospecifically performed via their silyl enol ethers, (e.g., Table I, **2d** and **2e**); (ii) selective α-chlorination of ketones having an extra olefin can be performed, leaving the extra olefin intact (e.g., Table I, **2f–i**). Although it has been shown[2] that ketones are chlorinated with cupric chloride in DMF to produce α-chloro ketones, the direct chlorination of unsymmetrical ketones gives mixtures of α- and α′-chloro ketones. Therefore, the present chlorination reaction of silyl enol ethers complements the direct chlorination of ketones.

Reaction of Silyl Enol Ethers with Anhydrous $FeCl_3$. Silyl enol ethers were also reacted with $FeCl_3$ in acetonitrile to give α-chloro ketones in moderate yields (Table I). The use of DMF, which was a crucial solvent for the chlorination with $CuCl_2$, brought about unsatisfactory results.

A large excess of $FeCl_3$ is necessary for the chlorination of silyl enol ethers. For example, the use of a 4 or 5 molar excess of $FeCl_3$ resulted in satisfactory yields of α-chloro ketones, but the use of a 2 molar excess of $FeCl_3$ gave lower yields of α-chloro ketones together with the regeneration of the starting ketones. It is noteworthy that unlike the chlorination with $CuCl_2$, the reaction of a silyl enol ether having an extra olefin with $FeCl_3$ afforded a mixture of α-chloro ketone (**2**), cyclic chloro ketone (**3**), and dimeric 1,4-diketone (**4**) (Scheme I). The ratio of these three products depends upon the reaction conditions employed. The formation of cyclic chloro ketone was more favored when the silyl enol ether was added at once to a refluxing solution of a 5 molar excess of $FeCl_3$ in acetonitrile and then quenched within 1 min. For instance, the reaction of 2-[(trimethylsilyl)oxy]-1,5-hexadiene (**1g**) with a 5 molar excess of $FeCl_3$ in acetonitrile afforded a mixture of 1-chloro-5-hexen-2-one (**2g**), 4-chlorocyclohexanone (**3g**),[3] and dodeca-1,11-diene-5,8-dione (**4g**)[4] in 10, 24, and 1%

(1) (a) Ito, Y.; Konoike, T.; Saegusa, T. *J. Am. Chem. Soc.* **1975**, *97*, 649–51. (b) Ito, Y.; Fujii, S.; Saegusa, T. *J. Org. Chem.* **1976**, *41*, 2073–4. (c) Ito, Y.; Saegusa, T. *Ibid.* **1977**, *42*, 2326. (d) Ito, Y.; Sugaya, T.; Nakatsuka, M.; Saegusa, T. *J. Am. Chem. Soc.* **1977**, *99*, 8366.

(2) Kosower, E. M.; Cole, W. J.; Wu, G.-S.; Cardy, D. E.; Meisters, G. *J. Org. Chem.* **1963**, *28*, 630–3.

(3) **3g**: IR (neat) 1720 cm^{-1}; NMR ($CDCl_3$ with Me_4Si) δ 2.0–3.0 (m, 8 H), 4.44 (m, 1 H).

(4) Ito, Y.; Konoike, T.; Harada, T.; Saegusa, T. *J. Am. Chem. Soc.* **1977**, *99*, 1487–93.

(5) (a) Cook, C. D.; Woodworth, R. C. *J. Am. Chem. Soc.* **1953**, *75*, 6242–4. (b) Bacon, R. G. R.; Hill, H. A. O. *Q. Rev., Chem. Soc.* **1965**, *19*, 95–125.

(6) Pouchert, C. J. "The Aldrich Library of Infrared Spectra", 2nd ed.; Aldrich Chemical Company Inc.: Milwaukee, WI, 1975.

(7) Warnhoff, E. W.; Martin, D. G.; Johnson, W. S. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. 4, pp 162–6.

0022-3263/80/1945-2022$01.00/0