(9) J. D. Roberts and R. H. Mazur, *J. Am. Chem. Soc.*, **73**, 2509 (1951).
(10) (a) D. I. Schuster, Ph.D. Dissertation, California Institute of Technology, 1961, p 97. (b) J. Verhulst, *Bull. Soc. Chim. Belg.*, **40**, 85 (1931).
(11) J. A. Moore and D. E. Reed, *Org. Synth.*, **41**, 16 (1961).
(12) M. Neeman, M. C. Caserio, J. D. Roberts, and W. S. Johnson, *Tetrahedron*, **6**, 36 (1959).
(13) H. C. Brown and M. K. Unni, *J. Am. Chem. Soc.*, **90**, 2902 (1968).
(14) (a) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, Wiley, New York, N.Y., 1967, p 1287; (b) *ibid.*, p 682.
(15) Y. E. Rhodes and L. Vargas, *J. Org. Chem.*, **38**, 4077 (1973). We thank Dr. Luis Vargas for the gift of a sample of cyclopropylacetic acid.
(16) Y. E. Rhodes and T. Takino, *J. Am. Chem. Soc.*, **90**, 4469 (1968); T. Takino, Ph.D. Dissertation, New York University, 1969, p 193.
(17) J. D. Roberts and V. C. Chambers, *J. Am. Chem. Soc.*, **73**, 5034 (1951).
(18) J. S. Swinehart, "Organic Chemistry: An Experimental Approach", Appleton-Century-Crofts Meredith Corp., New York, N.Y., 1969, p 22.
(19) R. R. Sauers and R. W. Ubersax, *J. Org. Chem.*, **31**, 495 (1966).

Reduction of *gem*-Dihalocyclopropanes with Zinc. Monoreductive Dehalogenation of *gem*-Dihalocyclopropyl Methyl Ketones and Dioxolanes

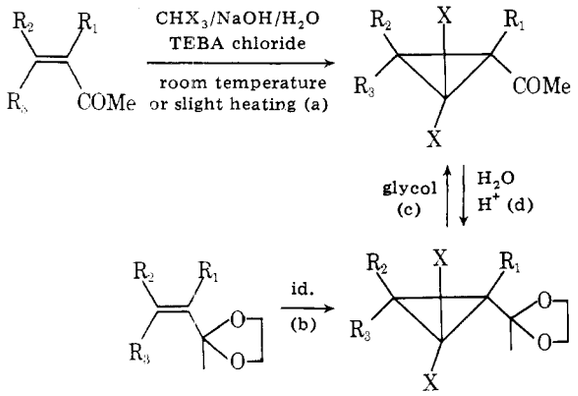
Roger Barlet

Laboratoire de Chimie Organique, Université Scientifique et Médicale de Grenoble, 38041 Grenoble, Cedex, France

Received June 1, 1977

The monoreduction, by means of zinc powder in alcoholic potassium hydroxide, of 11 *gem*-dihalocyclopropyl methyl ketones and six *gem*-dihalocyclopropylmethyldioxolanes was reported and gave satisfactory yields. With ketones, contrary to dioxolanes, the monoreduction occurred without general stereoselectivity, but required critical temperature control and precise reaction times to prevent total reduction. α-Alkylated ketones ($R_2 = R_3 = H$; R_1 = Me, *i*-Pr, or *t*-Bu) led predominantly to cis isomers, especially with bulky R_1, while α,β- ($R_3 = H$; R_1 = Me; R_2 = Me or *i*-Pr) and β,β′-dialkylated ketones ($R_1 = H$; $R_2 = R_3$ = Me) gave steric preference depending on the nature of the halogen. In all cases, dioxolanes gave a stereoselective formation of the trans isomers. These results were rationalized by postulating a predominant initial zinc attack at the less hindered C–X bond. With dioxolanes, the second step would be a high inversion of the resulting α-halocyclopropyl radicals. With ketones, intermediates could be carbanions and results explained by an easier inversion of the α-chlorocyclopropyl carbanions relative to the α-bromocyclopropyl carbanions.

A large variety of reagents can bring about reductive monodehalogenation of *gem*-dihalocyclopropanes.[1,2] Furthermore, recent studies examined the stereoselectivity of such a monoreduction with organotin hydride,[3-5] lithium aluminum hydride ($LiAlH_4$),[6,7] or related hydrides.[8,9] Moreover,



zinc powder in acetic acid[10] or ethanol–acetic acid[11] was revealed as an efficient and cheap means for reducing dihalocyclopropanes. The recent reduction with zinc in alcoholic potassium hydroxide appeared particularly attractive as a stereoselective and easy method.[2]

We wish now to report the monoreduction of *gem*-dihalocyclopropyl methyl ketones and their corresponding dioxolanes with this latter reagent. It was of interest to test the generality of the monoreduction, with a free or a protected carbonyl group as ring substituent, and to check its stereoselectivity especially with a crowded group such as a dioxolane.

The substrates were easily available by dihalocarbenic addition to olefinic ketones (a) or to dioxolanes (b) with subsequent ketalization (c) or hydrolysis (d) if needed.[12] The two-step procedure (a + c) for dioxolane synthesis was preferred to the direct addition (b). Conversely, for ketones, the direct method (a) was better except for compounds with $R_1 = H$, which required steps b and d.

Results

Results are summarized in Tables I and II. Our experimental conditions (method m_1) gave monoreduced rings as major products with satisfactory yields.

Ketones A–K (Table I) underwent reduction more easily than dioxolanes L–Q (Table II) with the exception of the dichloro ketone F, which was not reduced in boiling ethanol but required boiling propanol or butanol. It is also noteworthy that dibromo ketones underwent monoreduction more readily than dichloro ketones. In both cases formation of fully reduced cyclopropanes was difficult to avoid.

For ketones the extent of the reduction was greatly dependent on the temperature. In order to limit the reduction and to obtain preferably monoreduced ketones each substrate required specific temperature conditions and reaction time. Furthermore, for a few ketones we determined a critical temperature below which the extent of the reduction was considerably reduced and above which the complete reduction occurred rapidly. In all cases stereoisomeric pairs of cis and trans monoreduced compounds (cis and trans refer to the position of the halogen relative to the acetyl group) were obtained without general selection.

For dioxolanes, with careful temperature and reaction time controls we obtained a stereoselective monoreduction, giving predominantly the trans isomer.

Identification and Characterization

Identification and configurational assignments of the reduced compounds were easily achieved by comparison with halocarbenoid adducts of olefinic dioxolanes previously prepared.[13] Halocyclopropanation by halogen exchange gave both chloro- and bromodioxolanes which were converted, when

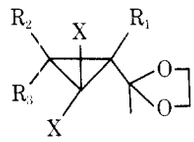
0022-3263/78/1943-3500$01.00/0

Table I. Monoreduction of *gem*-Dihalocyclopropyl Methyl Ketones

substrate					registry	temp,	time,	% yield mono-	% yield full	trans isomer	registry		cis isomer	registry		trans/cis
no.	R_1	R_2	R_3	X	no.	°C	h	redn	redn	no.	no.	%	no.	no.	%	(*t*/*c*)
A	Me	H	H	Cl	2568-72-1	60	20	90	0	**1t**	66793-70-2	35	**1c**	66788-39-4	65	0.53
B	Me	H	H	Br	2568-73-2	60	17	95	5	**2t**	52034-84-1	37	**2c**	64731-69-7	63	0.58
C	*i*-Pr	H	H	Cl	52100-72-8	60	30	80	0	**3t**	66788-35-0	30	**3c**	66788-40-7	70	0.43
D	*i*-Pr	H	H	Br	52100-82-0	40	25	75	0	**4t**	66788-36-1	20	**4c**	66788-27-0	80	0.25
						80	20	0	100							
E	*t*-Bu	H	H	Cl	52100-73-9	50	50[a]	40	15	**5t**[b]	66788-37-2	10	**5c**[b]	66788-28-1	90	0.11
F	Me	Me	H	Cl	52100-74-0	97	5	70	5	**6t**	66808-14-8	35	**6c**	66788-29-2	65	0.54
						110	5	50	25			50			50	
G	Me	Me	H	Br	52100-83-1	50	24	30	0	**7t**	62234-89-3	58	**7c**	66101-85-7	42	1.38
						53	18	70	30							
						60	18		100							
H	Me	*i*-Pr	H	Cl	52100-76-2	50	48	70	10	**8t**	66808-15-9	13	**8c**	66788-30-5	87	0.15
I	Me	*i*-Pr	H	Br	52100-85-3	50	15	50	50	**9t**	62234-90-6	55	**9c**	66808-13-7	45	1.22
J	H	Me	Me	Cl	3591-54-6	20	45	85	0	**10t**	66788-38-3	90	**10c**	66788-31-6	10	9.00
K	H	Me	Me	Br	52100-90-0	20	40	90	0	**11t**	66236-48-4	20	**11c**	66788-32-7	80	0.25
						45	6	75	0			50			50	1.00

[a] An increased reaction time did not give higher yields of monoreduced compounds. [b] **5t** and **5c** were not isolated and were identified by chromatographic analogy with other stereoisomer pairs.

Table II. Monoreduction of *gem*-Dihalocyclopropylmethyldioxolanes



substrate					registry	meth-	temp,	time,	% yield mono-	% yield full	trans isomer	registry		cis isomer	registry		trans/cis
no.	R_1	R_2	R_3	X	no.	od[a]	°C	h	redn	redn	no.	no.	%	no.	no.	%	(*t*/*c*)
L	Me	H	H	Cl	66788-33-8	m_1	60	15	75	0	**12t**	64731-81-3	62	**12c**	64731-82-4	38	1.63
						m_2	84	18	95	0			57			43	1.33
M	Me	H	H	Br	66788-34-9	m_1	80	90	90	10	**13t**	64731-53-9	65	**13c**	64731-54-0	35	1.85
N	H	Me	H	Cl	52100-78-4	m_1	80	6	95	5	**14t**	64731-55-1	72	**14c**	64753-84-0	28	2.57
O	H	Me	H	Br	52100-87-5	m_1	45	72	70	15	**15t**	64731-56-2	79	**15c**	64753-85-1	21	3.76
P	H	Me	Me	Cl	52100-80-8	m_1	80	15	100	0	**16t**	59083-00-0	64	**16c**	59082-99-4	36	1.77
						m_2	84	15	90	5			90			10	9.00
						m_3	65	15	30	7			75			25	3.00
						m_3	65	40	60	10			75			25	3.00
Q	H	Me	Me	Br	52100-89-7	m_1	45	50	85	15	**17t**	59083-02-2	77	**17c**	59083-01-1	23	3.35
						m_2	84	14	0	100							

[a] m_1 = Zn/EtOH/KOH; m_2 = $LiAlH_4$/DME; m_3 = $LiAlH_4$/THF.

needed, into corresponding ketones by final acid hydrolysis. (An example can be found in Scheme I.) Halocarbene addition on this starting olefinic dioxolane gave isomeric ratios similar to those obtained by reduction of L and M (**12t/12c** = 72:28 for halocarbene addition; **12t/12c** = 62:38, **13t/13c** = 57:43 for monoreduction). Conversely, reduction of A and B gave reversed ratios (**1t/1c** = 35:65, **2t/2c** = 37:63).

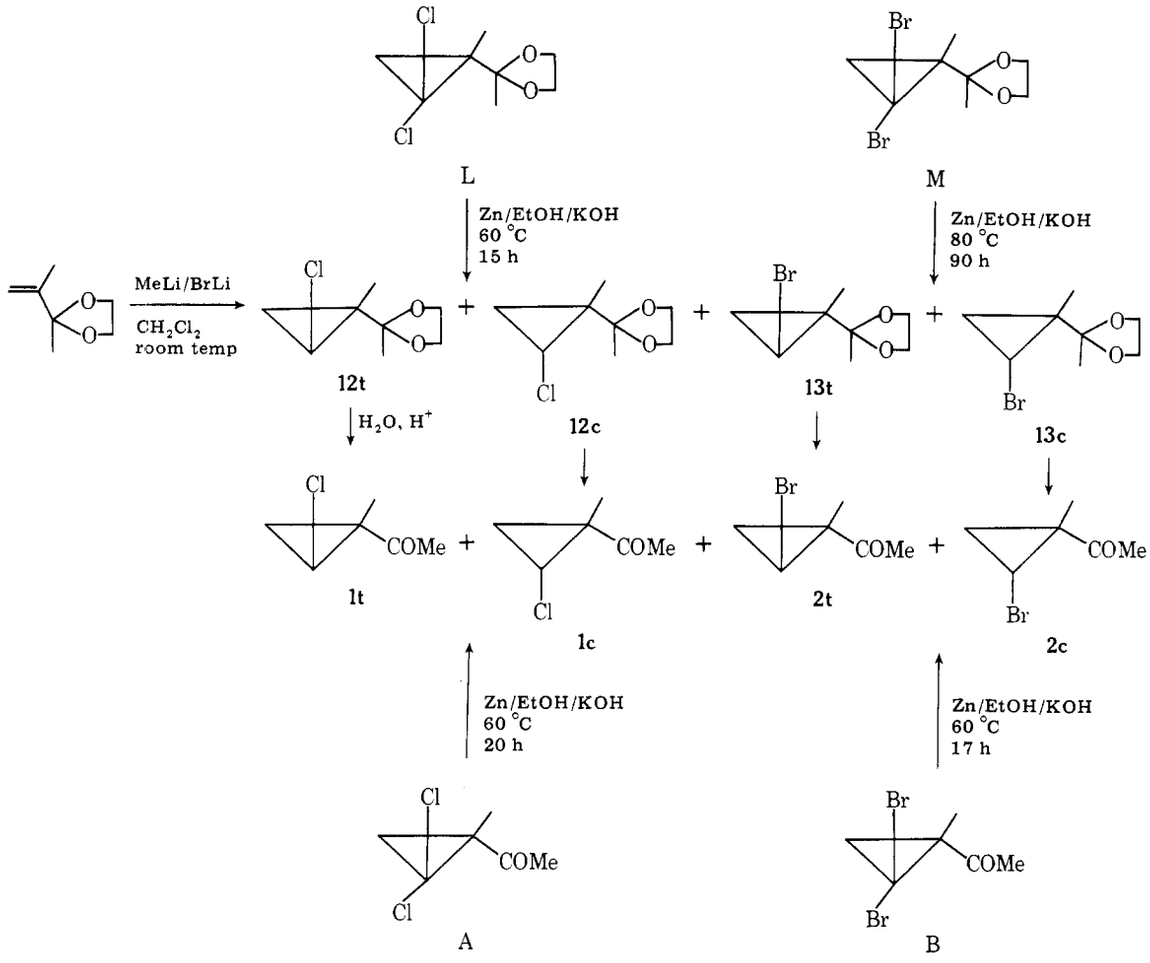
The isomeric ratios were estimated by gas chromatography, taking into account the molecular response factor of each stereoisomer.

2t, **7t**, and **9t** were recently described.[14] The other ketones are new compounds which gave satisfactory elemental analysis (Cl ± 0.3%, Br ± 0.5%).

The configurational assignments of the above compounds are supported by their NMR and IR spectral characterization (Table III): the values of the coupling constants $^3J_{vic}$ ($^3J_{trans}$ ~ 5 Hz, $^3J_{cis}$ ~ 8 Hz) for the two vicinal cyclopropyl protons with isomers **6t** to **11t** and **6c** to **11c**; the induced shifts by $Eu(dpm)_3$, higher for H_3 than for H_2 and H_4 with isomers **1c** to **4c** and lower for h_2 than for H_3 and H_4 with isomers **1t** to **4t**; the greater deshielding of the H_4 proton in trans isomers (diamagnetic anisotropy of the carbonyl group affecting the proton in the cis position more); the lower ν_{CO} absorptions for the trans isomers relative to the cis isomers (important halogen field effect when the halogen and the carbonyl are in cis position).[13]

The trans and cis configurations of the dioxolanes were also determined by the ^1H NMR chemical shift of the H_4 proton which showed, as in ketones, a greater deshielding and a lower $^3J_{vic}$ for the trans stereoisomer. However, the best distinction occurred again with corresponding methyl ketones (Table IV). The monoreduced stereoisomers **12** to **15** showed two $^3J_{vic}$ and the determination of configurations required the LIS effect, with $Eu(dpm)_3$, on the corresponding ketones.

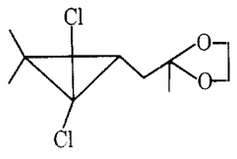
Scheme I



Discussion

The stereoselective reduction of dioxolanes appears easy to rationalize, but in the reduction of ketones the results cannot be explained as easily.

With dioxolanes the predominant formation of the trans isomer (t/c between 1.63 and 3.76) seems strongly dependent on steric factors. For instance, in comparative monoreduction of dichloro and dibromo compounds the stereoselectivity was larger with bromo compounds. On the other hand, when the buttressing dioxolane group is more distant from the halogens the stereoselectivity was reversed (t/c = 1.77 with P, 0.5 with R).



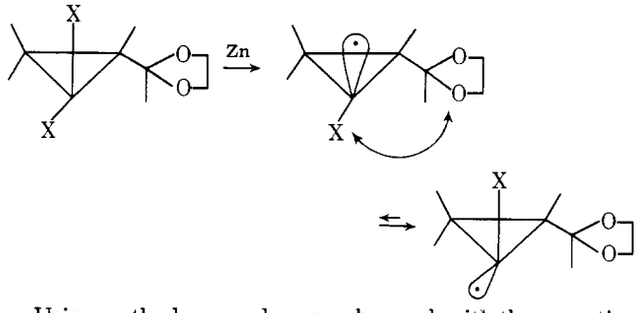
R

m_1, 80 °C, 26 h → trans isomer + cis isomer.

yield of monoreduction 100% — 33% — 66%

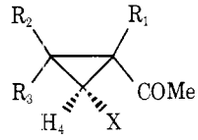
Previous zinc monoreductions of *gem*-bromofluorocyclopropanes proceeded with complete retention of configuration at low temperature and slight inversion at high temperature. Moreover, *gem*-dibromocyclopropanes gave the more hindered monoreduced cyclopropanes (syn stereoselection). To explain these results a three-step mechanism has been postulated:[2] (a) formation of interconvertible radicals with major retention of configuration (slow conversion occurring only at high temperature with α-fluorocyclopropyl radicals and possibly at lower temperature with more easily convertible α-bromocyclopropyl radicals); (b) further reduction of radicals toward unconvertible anion with retention of configuration (direct formation of anion being ruled out because such an intermediate would be rapidly protonated, due to the protic solvent used, before any inversion could occur); and (c) final protonation with solvent.

On the contrary, with our substrates, the less hindered monoreduced compounds were preferentially obtained. With respect to the preceding mechanism *our own results can be interpreted as a predominant attack of zinc metal at the less hindered C–Br bond followed by a high inversion of the resulting α-bromocyclopropyl radical.* The increased inversion of α-bromocyclopropyl radicals β-substituted with a dioxolane group as compared to the unsubstituted radicals would be ascribed to the effect of oxygens as previously suggested[15] and to the steric crowding between the dioxolane group and the cis halogen atom.



Using methods m_2 and m_3 we observed, with the exception of the ambiguous case of L, an increased trans preference (see

Table III. Spectroscopic Identification of Monohalocyclopropyl Methyl Ketones



chloro compd	bromo compd	chemical shifts, δ, ppm R1 (H_1, Me, *i*-Pr)	R2 (H_2, Me, *i*-Pr)	R3 (H_3, Me)	H_4CX trans	H_4CX cis	coupling constants, *J*, Hz $J_{H_1H_4}$	$J_{H_2H_4}$	$J_{H_3H_4}$	$J_{H_2H_3}$	IR absorption ν_{CO}, cm^{-1} trans	ν_{CO}, cm^{-1} cis
1t		1.38	0.66	1.60	3.38			5	7.5	5.6	1694	
1c		1.40	1.01	1.73		2.94		7.8	5.5	6.2		1706
	2t	1.55	0.89	1.82	3.33			5.3	8.2	5	1693	
	2c	1.43	1.09	1.75		2.85		7.7	5.7	6.6		1704
3t		1.00, 0.85	0.75	1.50	3.42			5	7.5	5.8	1694	
3c		0.96, 0.82	0.90	1.52		2.97		8	4.8	6.8		1705
	4t	1.05, 0.87	0.82	1.65	3.40			5.2	8	5.5	1692	
	4c	0.98, 0.80	0.93	1.54		2.93		7.8	4.8	7		1704
6t		1.34	1.09	1.65	3.52				7.8		1691	
6c		1.35	1.14	1.97		2.63			5.2			1703
	7t	1.37	1.09	1.62	3.52				7.5		1689	
	7c	1.37	1.15	2.00		2.55			5.2			1703
8t		1.41	1.05, 0.97	1.65	3.48				8		1692	
8c		1.37	1.07, 0.97	1.70		2.66			4.5			1703
	9t	1.45	1.08, 1.02	1.65	3.49				7.3		1690	
	9c	1.38	1.09, 1.02	1.70		2.59			5.5			1703
10t		1.95	1.11	1.33	3.42		5				1697	
10c		1.85	1.18	1.29		3.12	8.2					1703.5
	11t	1.99	1.14	1.35	3.41		4.8				1696	
	11c	1.94	1.21	1.29		3.12	8					1703

Table IV. Spectroscopic Identification of Monohalocyclopropylmethyldioxolanes

dioxolane	δ_{H_4}, ppm	$^3J_{trans}$, Hz	$^3J_{cis}$, Hz	corresponding ketone δ_{H_4}, ppm	$^3J_{trans}$, Hz	$^3J_{cis}$, Hz	ν_{CO}, cm^{-1}
12c	2.95	5	8	2.94	5.5	7.8	1706
12t	3.10	4.5	7.8	3.38	5	7.5	1694
13c	2.96	5	8.2	2.85	5.7	7.7	1704
13t	3.14	4.5	8	3.33	5.3	8.2	1693
14c	2.78	5	8	3.00	5	8.2	1705.5
14t	2.98	4.5	7.8	3.42	4.5	7.5	1697
15c	2.80	4.8	8	3.02	5.2	8	1704.5
15t	3.03	4.5	7.8	3.36	5	7.8	1695.5
16c	2.77		8.5	3.12		8.2	1703.5
16t	2.90	4.8		3.42	5		1697
17c	2.78		8.3	3.12		8	1703
17t	2.92	4.6		3.41	4.8		1696

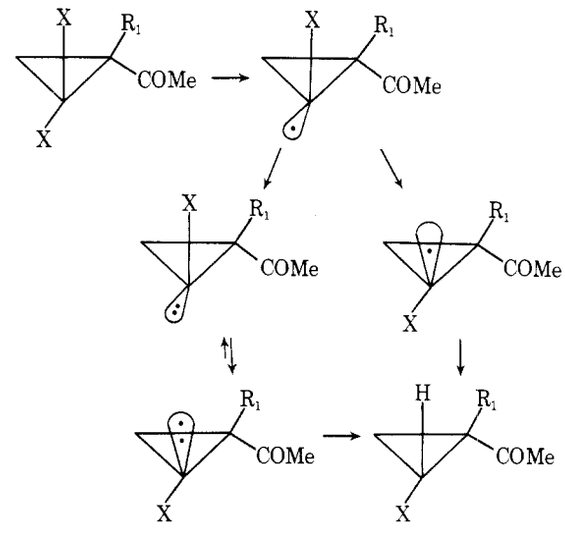
P in Table I and R below). The attack of the reagent at the less-hindered position remains, but it is probable that the direct intermediate is the carbanion[6] and that its inversion can take place in the absence of protic solvent and occurs more rapidly than with corresponding radicals.

$$R \xrightarrow[\substack{m_2,\ 14\ h,\ 84\ °C\\ m_3,\ 40\ h,\ 65\ °C}]{m_1,\ 67\ h,\ 80\ °C} \textbf{18t + 18c}$$

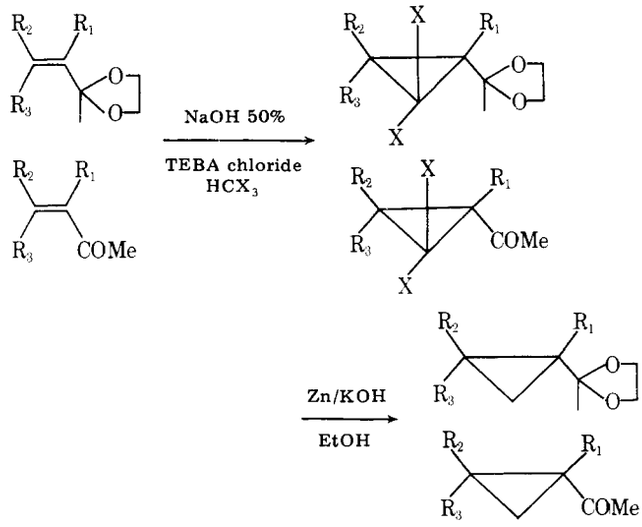
(t/c = 32:48 with method m_1, 48:52 with methods m_2 and m_3)

With ketones, the monoreduction results are very dependent on the ring alkylation and can again be rationalizated by postulating a predominant zinc attack at the less-hindered C–X and a possible inversion involving not only the ketonic radicals but also the ketonic carbanions. Indeed, the ketonic radicals, less strained than the dioxolane radicals, are stabilized and can undergo carbanions before inversion. We observed three different cases.

(1) With the α-alkylated dihalo ketones A–E the monoreduction occurred with an opposite stereoselectivity relative to dihalodioxolanes. Moreover, the increasing steric effect led to increased stereoselectivity (see the decrease of t/c with the increase of the size of R from Me to *t*-Bu). Attack by zinc



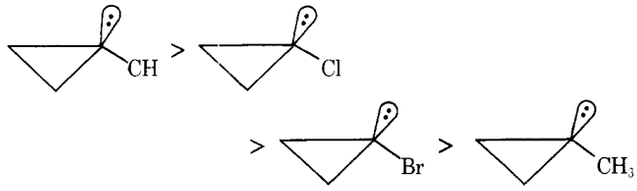
Scheme II



would occur at the halogen cis to the acetyl group since the latter, in a cisoid conformation,[16] is less bulky than R_1, particularly when R_1 = *i*-Pr or *t*-Bu.

(2) With the α,β-dialkyl dihalo ketones F–H, dichloro ketones led predominantly to cis isomers and dibromo ketones predominantly to trans isomers. These results are consistent with an enhanced zinc attack in position cis to the carbonyl and with a slower inversion of bromo carbanions.

(3) Conversely, with the β,β-dialkyl dihalo ketones I and J, the cis isomer was preferentially formed from dibromo ketone and the trans isomer from dichloro ketone. The major initial zinc attack would be reversed, due to steric effects, and followed by a more important inversion with the chloro carbanions. Slower inversion of the α-bromo carbanions vs. the α-chloro carbanions is compatible with previously reported results about carbanion stability.[3,17-18] According to these results we can write the following sequence of inversion barriers:



Moreover, the β-acetyl group will be a stabilizing group for α-chloro and α-bromo carbanions, allowing an intermediate inversion rate.

For synthetic purposes it is interesting to note that, with this reducing agent, in addition to the monoreduction, *gem*-dihalocyclopropyldioxolanes or ketones can lead to completely reduced compounds if no proper precautions are taken. Thus, the easily available starting compounds and the easy total reduction with zinc can allow the formation of cyclopropyl ketones or dioxolanes of any substitution (Scheme II). The dihalocarbonic addition to ketones gives higher fields, but fails with R_1 = H.[12] In the latter case it is necessary to utilize olefinic dioxolanes.

Experimental Section

Infrared spectra were recorded from thin liquid films on Perkin-Elmer 237 or 521 instruments. ^{1}H NMR spectra were obtained on a Perkin-Elmer R-10 nuclear magnetic resonance spectrometer.

General Procedure. Typically, the ketones or the corresponding dioxolanes (2 g) were added to ethanolic potassium hydroxide (10%, 20 mL) and stirred with zinc powder (6 g). Overall comparison showed that ketones were reduced more easily than dioxolanes and that total reduction was avoided only with moderate reaction temperature. Comparatively to dioxolanes, temperature and time reaction of monoreduction of ketones required greater control (Table I), but this reduction proved to be equally general.[19] As examples we can describe the preparation of **7t** and **7c** for ketones and general methods m_1, m_2, and m_3 for dioxolanes.

Table V. Values of Δ (hertz) for 1c,t–4c,t

isomers	R	X	H_4	H_3	H_2
1c	Me	Cl	492	1055	498
1t	Me	Cl	900	996	468
2c	Me	Br	510	1086	510
2t	Me	Br	905	1000	462
3c	*i*-Pr	Cl	460	1075	510
3t	*i*-Pr	Cl	1055	1085	450
4c	*i*-Pr	Br	475	1100	520
4t	*i*-Pr	Br	1055	1110	450

Table VI. Evaluation of Δ for Protons H_3 and H_4 in Ketones Corresponding to Dioxolanes 14c,t and 15c,t

	corresponding ketones		
dioxolanes	X	ΔH_3	ΔH_4
14c	Cl	894	432
14t	Cl	810	720
15c	Br	918	450
15t	Br	780	720

***cis*- and *trans*-1-Acetyl-2-bromo-1,3-dimethylcyclopropanes (7t and 7c).** 1-Acetyl-2,2-dibromo-1,3-dimethylcyclopropane (G; 2 g, 7.4 mmol) was mixed with zinc powder (6 g) and ethanolic potassium hydroxide (10%, 20 mL). The reaction was followed by VPC and after 18 h at 53 °C the yield of the monoreduction increased no more and reached 70%, while a large amount of total reduction (30%) was unavoidable. With a lower reaction temperature (50 °C) total reduction was avoided, but the monoreduction was greatly slowed down and reached only 30% after 24 h of reaction. With a higher reaction temperature (60 °C) only total reduction was observed. The reaction mixture was then filtered and 200 mL of water was added to the filtrate. After extraction of the aqueous layer with ether, added organic layer and ethereal extract were neutralized with an ammonium chloride solution and then dried and concentrated in vacuo.

Method m_1. The starting crude dioxolane[20] (2 g, 6.3–9.5 mmol) was added to an ethanolic potassium hydroxide and zinc powder mixture. This mixture was stirred for a variable time (6–90 h) and generally with refluxing ethanol temperature.[21] Extraction and separation were unchanged compared with ketones.

Method m_2. The starting dioxolane (2 g) was stirred with lithium aluminium hydride ($LiAlH_4$; 0.5 g, 13 mmol) and 25 mL of refluxing DME was carefully dried over potassium hydroxide. After about 15 h of reaction a few drops of water were added, permitting separation of organic layer and mineral aggregate. After neutralization by ammonium chloride solution the organic layer was dried and concentrated in vacuo with slight warming.

Method m_3. Similar to method m_2 except THF replaced DME.

Characterization. In a general way dibromodioxolanes appeared more susceptible to total reduction than dichlorodioxolanes. It was difficult to isolate monohalodioxolanes with a satisfactory purity. Indeed, often they were transformed into corresponding ketones during the chromatographic isolation. Consequently satisfactory elemental analyses were obtained only with ketones (Cl ±0.3%, Br ± 0.5%). However, by analytical chromatography with the use of moderate injector temperature, it was easy to observe the products of reduction without decomposition. Comparison with retention times of monohalocarbenoïc adducts of olefinic dioxolanes and transformation into corresponding ketones[13] allowed unambiguous identification of these monoreduced dioxolanes.

In VPC it is noteworthy to note that trans stereoisomers always show retention times smaller than cis stereoisomers.

Configuration. Lanthanide Induced Shifts (LIS Effect). Determination of the configuration for **1c** to **4c** and **1t** to **4t** required study of the LIS effect. Relative shifts of protons, after addition of $Eu(dpm)_3$, in a molecule containing a complexation center such as a carbonyl, is a very useful tool for this determination.[22] Halogens were not involved in the complexation[23] and the LIS effect allowed unambiguously the attribution of configuration for monohalo-substituted compounds **1–4**. The slope, Δ, of the equation

$$\delta_i = \delta_c - \delta_0 = f(C_{Eu}/C_0)$$

where δ_0 = shift without chelate, C_{Eu} = molar concentration of chelate, δ_c = shift with chelate, and C_0 = molar concentration of halo-

ketone, is characteristic for each proton.[24] Δ is higher for H_3 than for H_4 and H_2 with isomers **1c** to **4c** and lower for H_2 than for H_3 and H_4 with isomers **1t** to **4t**. Values of Δ (in hertz) are given in Table V.

Likewise, for the determination of the configurations of dioxolanes we used the LIS effect of corresponding ketones. The configuration of dioxolanes **12t**, **12c**, **13t**, and **13c** was determined by the study of ketones **1t**, **1c**, **2t**, and **2c**. We assigned the configuration of dioxolanes **14c**, **14t**, **15c**, and **15t** by the evaluation of Δ for protons H_3 and H_4 in corresponding ketones (Table VI).

Acknowledgment. We wish to thank Dr. U. O. Cheriyan and Professor R. J. Taillefer of the University of Sherbrooke for their assistance in the English rewriting of this article.

Registry No.—Zinc, 7440-66-6.

References and Notes

(1) R. Barlet and Y. Vo-Quang, *Bull. Soc. Chim. Fr.*, 3729 (1969).
(2) H. Yamanaka, R. Oshima, K. Teramura, and T. Ando, *J. Org. Chem.*, **37**, 1734 (1972).
(3) J. Hatem and B. Waegell, *Tetrahedron Lett.*, 2019 (1973).
(4) G. Leandri, H. Monti, and M. Bertrand, *Tetrahedron*, **30**, 283 (1974).
(5) T. Ishihara, E. Ohtani, and T. Ando, *J. Chem. Soc., Chem. Commun.*, 367 (1975).
(6) C. W. Jefford, U. Burger, M. H. Laffer, and N. Kabengele, *Tetrahedron Lett.*, 2483 (1973).
(7) J. Hatem and B. Waegell, *Tetrahedron Lett.*, 2023 (1973).
(8) L. Sydnes and L. Skattebol, *Tetrahedron Lett.*, 3703 (1974).
(9) J. T. Groves and K. W. Ma, *J. Am. Chem. Soc.*, **96**, 6527 (1974).
(10) A. Leray, H. Monti, M. Bertrand, and H. Bodot, *Bull. Soc. Chim. Fr.*, 1450 (1968); H. Monti and M. Bertrand, *Tetrahedron*, **29**, 2821 (1973).
(11) R. E. Erickson, R. Annino, M. D. Scanlon, and G. Zon, *J. Am. Chem. Soc.*, **91**, 1767 (1969).
(12) R. Barlet, *C.R. Hebd. Seances Acad. Sci., Ser. C*, **278**, 621 (1974).
(13) R. Barlet and M. Vincens, *Tetrahedron*, **33**, 1291 (1977).
(14) R. Barlet, *Tetrahedron Lett.*, 4171 (1976).
(15) T. Ando, H. Yamanaka, F. Namigata, and W. Funasaka, *J. Org. Chem.*, **35**, 33 (1970).
(16) R. Barlet, *Bull. Soc. Chim. Fr.*, 545 (1977).
(17) H. M. Walborsky, F. J. Impastato, and A. E. Young, *J. Am. Chem. Soc.*, **86**, 3283 (1964).
(18) H. M. Walborsky and F. M. Hornyak, *J. Am. Chem. Soc.*, **77**, 6026 (1955).
(19) With the exception of the *trans*-1-acetyl-2,2-dibromo-3-methylcyclopropane obtained from dioxolane O, which gave probably a substitution product after the reduction with incorporation of an ethoxy group in the isolated product of reaction.
(20) Crude materials, from dihalocyclopropanation, are used as starting dioxolanes because they are easily decomposed into their corresponding ketones by distillation or chromatographic isolation. However, their assay by analytical chromatography showed a satisfactory purity.
(21) With exceptions for O and especially Q, which are fully reduced into the cyclopropane derivatives with boiling ethanol.
(22) (a) J. P. Begue, *Bull. Soc. Chim. Fr.*, 2073 (1972); (b) J. Bouquant and J. Chuche, *Tetrahedron Lett.*, 2337 (1972); (c) R. Von Ammon and R. D. Fisher, *Angew. Chem., Int. Ed. Engl.*, **11**, 675 (1972); (d) A. F. Cockerill, G. L. O. Davies, R. C. Harden, and D. M. Rackhan, *Chem. Rev.*, 443 (1973); (e) B. C. Mayo, *Chem. Soc. Rev.*, 49 (1973).
(23) J. K. M. Sanders and D. H. Williams, *J. Am. Chem. Soc.*, **93**, 641 (1971).
(24) P. V. Demarco, T. K. Ezley, R. B. Lewis, and E. Wenkert, *J. Am. Chem. Soc.*, **92**, 5734, 5739 (1970).

Side-Chain Inversion of Steroidal Olefins Promoted by Hydrogen Chloride

Mario Anastasia,* Alberto Fiecchi, and Antonio Scala

Institute of Chemistry, Faculty of Medicine, University of Milan, I-20133 Milano, Italy

Received December 29,1977

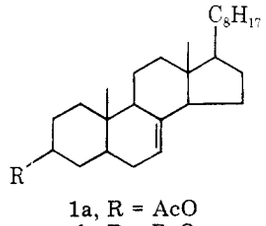
The reaction of hydrogen chloride on 7-, 8(14)-, and 14-ene steroids was investigated. A 14α-chloro compound is the product of kinetically controlled addition of the acid. A 14β-chloro compound with the side chain in the 17α configuration originates in diethyl ether at temperatures lower than −30 °C in the presence of hydrogen chloride, via a carbocation at C_{14}. There is evidence that the inversion occurs through two distinct rearrangements involving the intermediary formation of a 12,14α-cyclo-12,13-seco-5α-cholest-13(17)-ene.

In a previous communication[1] we reported that 3β-acetyloxy-5α-cholest-7-, -8(14)-, or -14-enes (**1a, 2a,** and **3a**) undergo inversion of the side chain by the action of hydrogen chloride in diethyl ether at −60 °C to yield 3β-acetyloxy-14-chloro-5α,14β,17β*H*-cholestane (**4a**), possibly through the intermediary formation of 3β-acetyloxy-12,14α-cyclo-12,13-seco-5α-cholest-13(17)-ene (**5a**). Caspi et al.[2] simultaneously described the isolation of 3β-acetyloxy-5α,17β*H*-cholest-14-ene (**6a**) by the action, on **2a,** of hydrogen chloride in chloroform at −78 °C and prolonged treatment with $NaHCO_3$. More recently it has been shown that the same rearrangement is also caused by hydrogen bromide.[3]

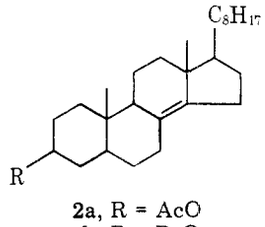
In order to clarify the mechanism of the side chain inversion, we decided to explore the processes involving the action of hydrogen chloride on 7-, 8(14)-, and 14-ene steroids.

Hydrogen chloride has long been considered to promote the direct isomerization of the 7 or 8(14) double bond of steroids to the 14 position.[4] In fact 14- and 8(14)-ene steroids in an approximately 1:1 ratio were isolated when the reaction was carried out at 0 °C in chloroform solution.[5] However Cornforth et al.,[6] operating at −30 °C on 3β-benzoyloxy-5α-cholest-8(14)-ene (**2b**), isolated a compound to which the structure of 3β-benzoyloxy-14α-chloro-5α-cholestane (**7a**) was attributed. When a chloroform solution containing this adduct was shaken with aqueous $NaHCO_3$, dehydrochlorination occurred and 3β-benzoyloxy-5α-cholest-14-ene (**3b**) was obtained.

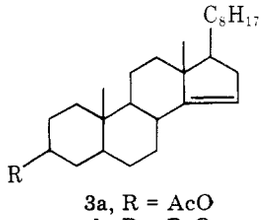
In order to definitively prove that the 14-ene (**3b**) is never formed by the direct action of hydrogen chloride on 8(14)-ene



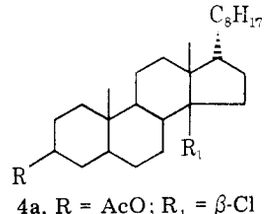
1a, R = AcO
b, R = BzO



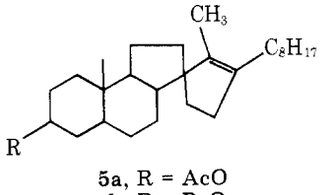
2a, R = AcO
b, R = BzO



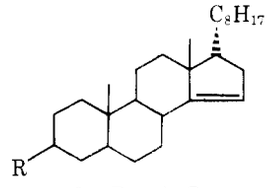
3a, R = AcO
b, R = BzO



4a, R = AcO; R_1 = β-Cl
b, R = BzO; R_1 = β-Cl
c, R = AcO; R_1 = β-H



5a, R = AcO
b, R = BzO



6a, R = AcO
b, R = BzO