

INTRAMOLECULAR CYCLIZATION OF CYCLOALKENE CARBOXYLIC ACID CHLORIDES

ANDREAS HEUMANN[†] and WOLFGANG KRAUST[‡]

Department of Chemistry, University of Tübingen, D-7400 Tübingen, Germany

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Abstract—Thermal cyclization of cyclooctene-4-yl-carboxylic acid chloride (5) and cycloheptene-4-yl-carboxylic acid chloride (10) yielded mixtures of mainly *endo* and *exo* 2-chlorobicyclo[3.3.1]nonane-9-one (7 and 8), and mixtures of *endo* and *exo* 2-chlorobicyclo[3.2.1]octane-8-one (12 and 13), respectively. AlCl_3 -catalyzed cyclization of 10 gave the same product composition as the uncatalyzed reaction. In the AlCl_3 -catalyzed cyclization of 5 considerable amounts of bicyclo[3.3.1]non-2-en-9-one (6) and *exo* 3-chlorobicyclo[3.3.1]nonane-9-one (9) were obtained in addition to 7 and 8.

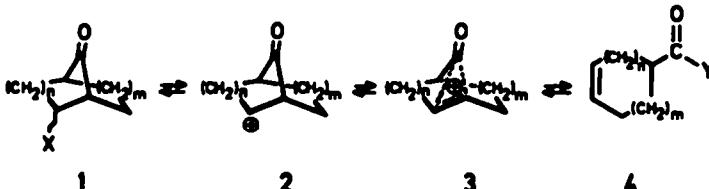
During the past 15 years the stereochemistry of the Friedel-Crafts acylation of double bonds¹ has been investigated using several bicyclic compounds.²⁻⁴ Stereoselective intramolecular *cis*⁵ and *trans*⁶ additions as well as formation of epimers has been observed, depending on the reaction conditions.⁴⁻⁶ In certain cases, intramolecular Friedel-Crafts acylation may compete with ketene cycloaddition.⁷ Despite the fact that this reaction seems to be a very useful method for the preparation of bicyclic derivatives, particularly in the bicyclo[3.3.1]nonane series,^{4,8} systematic studies on catalysis and solvent effects on various model compounds have not been reported. Consequently, important questions remain to be answered regarding the overall mechanism of this reaction.

We have been interested for some time in the synthesis and fragmentation of functionalized bicyclic compounds, particularly those of the bridged bicyclooctanyl and bicyclononanyl type.^{9,10} In order to get more detailed information concerning reaction intermediates such as 2 and 3 we initiated a comprehensive study on cyclization reactions of monocyclic unsaturated acid chlorides under different reaction conditions. The conceivable intermediary bicyclic cations can be generated either by solvolyzing bicyclic ketotosylates^{11,12} ($1 \rightleftharpoons 2 \rightleftharpoons 3$) or by an intramolecular electrophilic reaction of an acid halide to a double bond ($4 \rightleftharpoons 3$).¹⁻³

isomeric reaction products. In the presence of water, norbornane and bicyclo[3.2.1]octane derivatives undergo ring opening¹¹⁻¹³ to give the corresponding unsaturated monocyclic carboxylic acids, whereas in the case of bicyclo[3.3.1]nonane-9-one-2-yl tosylate no fragmentation is observed.¹¹ Other processes probably depend upon strain factors in the bridging carbonyl. The marked difference in reactivity between bicyclooctanone and bicyclononanone compounds, however, may be due to some important variations in stability of possible ionic intermediates in these two systems. The serious complications in the interpretation of the mechanism of the solvolytic generation of conceivable intermediates such as 2 or 3 lead us to study the intramolecular addition of acid chlorides to C=C double bonds. Erman and Kretschmar¹⁴ found that cyclooct-4-*cis*-ene-1-carboxylic acid chloride (5) can be cyclized to give the epimeric chlorides 7 and 8 of bicyclo[3.3.1]nonane-9-one. Detailed investigations on the mechanism of this reaction carried out in our laboratory which include the extension of the reaction to cycloheptene acid chloride (10) has yielded considerable new information which we now report.

RESULTS

1. *Cyclization reactions.* Cyclooct-4-*cis*-ene-1-carboxylic acid chloride (5) can be easily cyclized



As described earlier¹¹ the solvolytic reactivity of bicyclo[3.2.1]octane and bicyclo[3.3.1]nonane tosylates is low corresponding to 1. Product analyses showed more than 80% of unarranged starting material and 20% of

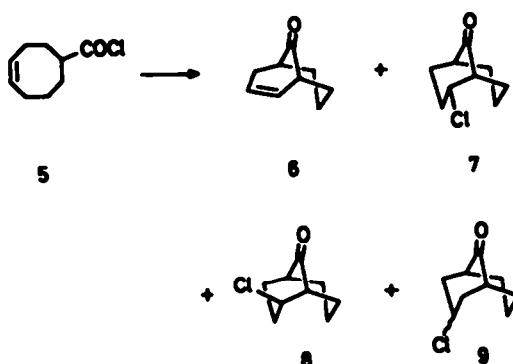
under different reaction conditions (Table 1). All products have been isolated and purified by column chromatography on silica gel. Reducing of 5 in CCl_4 and working up by simple evaporation of the solvent (entry 1) lead within 10 days to a mixture of *endo* and *exo* 2-chloro-bicyclo[3.3.1]nonane-9-one (7 and 8) in a 3:2 ratio accompanied by small amounts of bicyclo[3.3.1]non-3-ene-9-one (6). The course of the reaction was monitored by NMR spectroscopy, which was facilitated because of good separation of the olefinic protons in 5 and the CH_2Cl -protons in 7 and 8, as well as by the fact

[†]New address: Laboratoire de Stéréochimie, Faculté St. Jérôme, F 13013 Marseille, France.

[‡]New address: Lehrstuhl für Organische Chemie der Universität Hohenheim, D-7000 Stuttgart 70, Germany. Correspondence should be sent to this author.

Table 1. Cyclization of cyclooct-4-cis-ene-1-carboxylic acid chloride (5)

Entry	Solvant	Catalyst	Time	Temp.	Total yield	Isolation	Reaction products (%)			
							6	7	8	9
1 ^a	CCl ₄	—	10 days	reflux (=77°)	quant.	Column chromatogr.	8	58	34	—[c]
2 ^a	dichloro-ethane	—	12 hr	reflux (=83°)	80-90%	Sublimed	7	58	35	—[d]
3 ^a	CCl ₄	AlCl ₃ (1.05 mole)	5 min	50°	80-90%	gic	25	57	13	5[c]
4 ^a	CCl ₄	AlCl ₃ (1.05 mole)	2 hr	10-25°	80-90%	gic	13	54	17	16[c]
5 ^a	CCl ₄	AlCl ₃ (1.2 mole)	25 hr	15°	80-90%	Column chromatogr.	24	2	20	53[c]
6 ^a	CCl ₄	AlCl ₃ (2.1 mole)	20 hr	25°	80%	Sublimed	48	11	14	27[c]
7 ^a	dichloro-ethane	—	72 hr	reflux	?	Distilled	5	16	41	—
8 ^a	diglyme	AlCl ₃ cat.	16 hr	100°	?	Distilled	18-19	20-26	6-8	—
9 ^a	diglyme	BF ₃ ·Et ₂ O	27 hr	100°	25%	gic	53	3	5	—

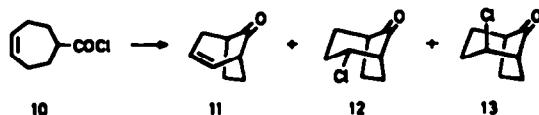
^aThis work.^bResults of Erman and Kretschmar, Ref. 4^a.^cProduct ratio detected by gic (6 = peak 1, 7 = peak 2, 8 = peak 4, 9 = peak 3).^dProduct ratio detected by NMR.

that only small amounts of 6 were formed. When carbon tetrachloride (b.p. 77°) was replaced by 1,2-dichloroethane (b.p. 83-84°) the reaction time decreased dramatically from 10 days to 12 hr or less (entry 2). The mixture showed nearly the same product ratio and the *endo* chloride (7) remained as the predominant product. In contrast to cyclization in CCl₄, the crude mixture must be purified by sublimation after evaporating of the dichloroethane solvent in order to get a resolved and interpretable NMR spectrum.

Quite different results were observed when the cyclization was carried out with stoichiometric amounts of anhydrous AlCl₃ in CCl₄. 7 remained as the main product, when the reaction was stopped after a short time (5 min to 1 or 2 hr, entry 3 and 4) but in addition to 6 and 8 AlCl₃ caused the formation of a new compound, namely 9. This compound predominated after 25 hr time, while 7 disappeared nearly completely (entry 5). The formation of olefin (6) increased with increasing amounts of added AlCl₃ (entry 6). These results may be compared with those obtained by Erman and Kretschmar^{4a} which have been included in Table 1 (entry 7-9). The different product ratios described in entry 2 compared to entry 7

are probably due to different working up procedures. The AlCl₃-catalyzed reaction (traces of AlCl₃) in diglyme (entry 8) may be rationalized as a thermal cyclization not completed after a 16 hr time. In our experiments we were not able to find any reaction leading to the *exo*-chloride (8) as the main product.

Markedly different results were obtained with cyclohept-4-cis-ene-1-carboxylic acid chloride (10): No difference in the product ratio could be detected between the thermal reaction and the reaction with molar quantities of AlCl₃. Both reactions gave high yields of mixtures consisting of 93% *endo*-2-chloro-4-oxabicyclo[3.2.1]octane-8-one (12) and 7% *exo*-chloride (13).¹⁴ At best traces of bicyclo[3.2.1]oct-2-ene-8-one (11) were detectable, and a reaction time of 24 hr did not alter the product ratio in the AlCl₃-catalyzed reaction (Table 2).



2. Identification of reaction products. Compounds 6, 7 and 8 have been described and well characterized by Erman.^{4a} Additionally 7 and 8 are available by reaction of POCl₃ with a mixture of the corresponding epimeric alcohols 14 in anhydrous pyridine.¹⁵ The structure of 9 as a 3-chloro-4-oxabicyclo[3.3.1]nonane-9-one was derived from chemical and spectroscopical properties. Treatment of 9 with 10% NaOH in methanol gave bicyclo[3.3.1]non-

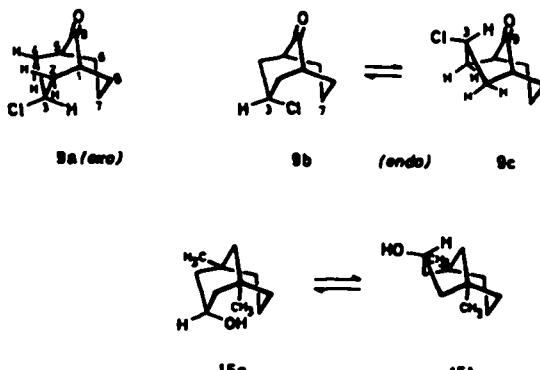


Table 2. Cyclization of cyclohept-4-cis-ene-1-carboxylic acid chloride (10)

Solvent	Catalyst	Time	Temp.	Total yield (%)	Isolation	Reaction products (%)	
						12 ^a	13 ^a
CCl ₄	—	2 days	reflux (77°)	100	Sublimation	93	7
CCl ₄	AlCl ₃ (1.1 mol)	1 hr	25°	80-90	Sublimation	93	7
CCl ₄	AlCl ₃ (1.1 mol)	24 hr	15-20°	80-90	Sublimation	93	7

^aProduct ratio detected by glc.

- 2 - ene - 9 - one (6). A rather complex signal for the CHCl-proton of 9 in the ¹H-NMR spectrum with a band width of 40-45 Hz ($W_{1/2}$ 18 Hz) at 4.93 ppm might be resolved as an asymmetric nine line pattern, corresponding to an A₂B₂X or AA'BB'X spectrum. Furthermore the symmetric structure of 9 is supported by six ¹³C absorptions in the ¹³C-NMR spectrum (Table 3).¹⁶ These data are in accordance with a C_{2v} symmetry of the bicyclo[3.3.1]nonane skeleton indicating that the chlorine atom is attached to C₃. At present we cannot establish the stereochemistry of 9 unequivocally without having both possible isomers at hand. Because of the short distance between C₃ and C₁ in an ideal chair-chair conformation¹⁷ *endo* 3-substituted derivatives of bicyclo[3.3.1]nonane show a chair-boat equilibrium (cf. 9a=9c; 15a=15b).⁸ Parker¹⁸ has estimated that *endo* bicyclo[3.3.1]nonane-3-ol (15) exists predominantly (86%) as a chair-boat form 15b in the conformation equilibrium 15a=15b. The "bow sprit flagpole" interaction operating in 15b, is relieved in structure 9c which bears a CO group at C₃, instead of CH₂. Therefore we should find 9 an *endo* isomer in the boat-chair form 9c as the exclusive conformer. This fact implies that the multiplicity of the ¹H-NMR signal for H₃ in 9a should nearly be the same as in 9c. I.e. 9a and 9c cannot be distinguished from each other by ¹H-NMR.^{16,19}



A somewhat better description is available from the ¹³C-NMR spectra.¹⁶ The γ -effect is supposed to be a sensitive indicator for stereochemical effects,²⁰ and in the case at hand it involves the chlorine atom at C_{1,3} of -1.8 ppm (Table 3). This value indicates little steric interaction between C₃-Cl and C₁-H(C₃-H). For this as well as for an electronically influenced (W-type) interaction both molecules 9a and 9c show little or no differences. The signal for C₃ at 20.9 ppm, however, and the small difference to the corresponding signal in bicyclo[3.3.1]nonane - 9 - one of 0.5 ppm, lead us to assume

Table 3. ¹³C-shifts from compound 9^a

	C _{1,3}	C _{2,4}	C ₃	C _{6,8}	C ₇	C ₉
[b]	44.6	43.5	53.2	34.1	20.9	217.6
[c]	-1.8	9.3	32.8	-0.1	0.5	-4.0

^aIn CDCl₃, values based on CDCl₃ signal, and transformed relative to TMS using equation $\delta_{\text{TMS}} = \delta_{\text{CDCl}_3} - 77.1$ ppm; a negative sign denotes a highfield shift.

^bRelative to TMS.

^cRelative to bicyclo[3.3.1]nonane-9-one,¹⁶ the values are caused by the α -effect (C₃), β -effect (C_{2,4}) and γ -effect (C_{1,3}), resp., of the chlorine substituent.

the structure corresponding to a sterically less hindered *exo* isomer 9a.²¹



Cyclization products of cyclohept - 4 - cis - ene - 1 - carboxylic acid chloride (10) have been characterized by NMR using double resonance and chemical reactions. Base cleavage of the *endo* chloride (12) with methanolic KOH gave cyclohept - 4 - cis - ene carboxylic acid (cf. Ref. 3). *Exo* chloride (13) is stable under these conditions, but conversion to bicyclo[3.2.1]oct - 2 - ene - 8 - one (11)²² occurs using more drastic conditions. The NMR pattern of CHCl of both the reaction mixture of 10, containing mainly 12 (*endo*), and of the isolated compound 13 are shown in Fig. 1. Since 13 was formed to the extent of up to 7% during cyclization reactions (Table 2), 12 and 13 were prepared by treatment of an *exo/endo* mixture of the corresponding alcohols 16 with POCl₃/pyridine in high yield. Both isomers are readily separated on silicagel.

DISCUSSION

Two mechanisms have been proposed by Erman and Kretschmar²³ for the cyclization of cyclooct - 4 - cis - 1 - carboxylic acid chloride (5): Based on the product ratio (Table 1) and the difference between the thermal (mainly *cis*-addition) and the AlCl₃-catalyzed (traces of AlCl₃) reaction (mainly *trans*-addition) the ion pairs 17, 18 or a free ion 19 are suggested as reaction intermediates.

In the first case the product ratio depends on the rate ratio for rearrangement 17 \rightarrow 18 and the collapse of 17 \rightarrow 8 (*exo* product) after kinetically controlled formation of 17. The presence of AlCl₃ causes more rapid dissociation and rearrangement of *exo* chloride ion pair 17 to *endo*

60 MHz

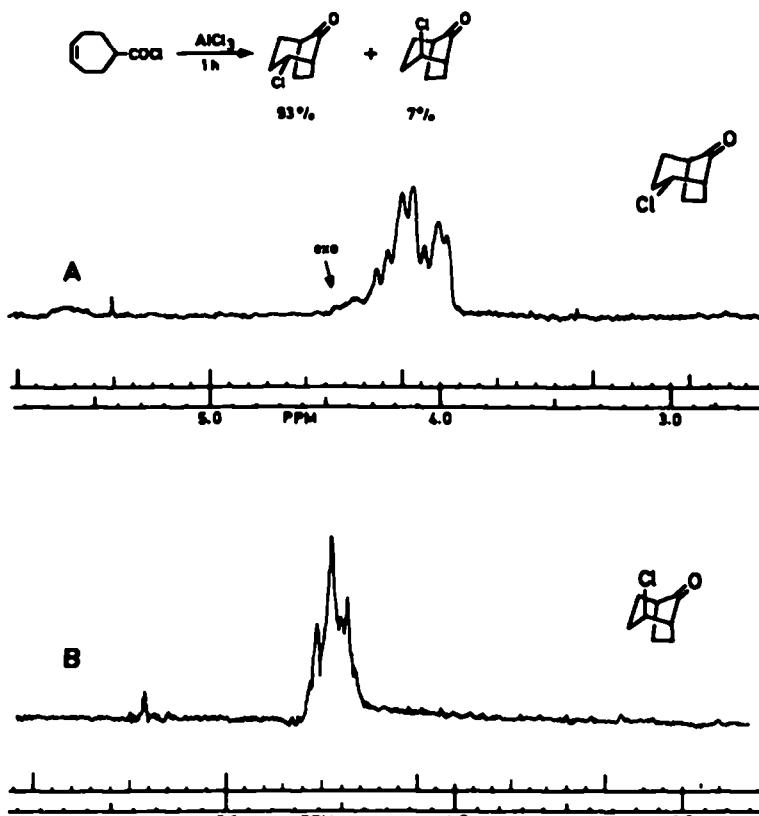


Fig. 1. ^1H -NMR spectrum (60 MHz) of CHCl pattern of 12 and 13. A: Mixture of cyclization products 12 (93%) and 13 (7%) from 10; B: 13, isolated from A by fragmentation procedure.



chloride (7) through ion pair 18. In contrast the absence of catalyst favours the rapid collapse of 17 to *exo* product 8. A second possible mechanism involves a free carbonium ion 19 which is substituted much easier from the *exo* side during thermal cyclization, while AlCl_3 in complexation with the CO group reverses the attack of Cl^- or AlCl_4^- towards the *endo* side.

Our results on the reactions of 5 permit us to conclude that the mechanistic pattern proposed by Erman should be modified in some respects. As may be seen from Table 1 it seems reasonable to consider separately two kinds of reactions. Thus there is a pure thermal reaction proceeding as a *trans* addition in the short time AlCl_3 -reaction yielding mainly *endo* chloride (7).²³ On the other hand the longer time AlCl_3 -reaction causes the formation of 3-chloro-bicyclo[3.3.1]nonane-9-one (9), (probably *exo*) as a product derived from hydride shift in the intermediate.²⁴ This stands in contrast to the results of Erman and Kretschmar²⁴ who do not report 9 as a product. Accordingly any mechanism for the overall process must also take this compound into consideration. Specifically, the difference in products between the thermal and AlCl_3 -reaction is not reported²⁴ only in

stereochemistry at C_2 but formation of an isomer namely 9. Therefore we conclude that a hydride shift is important in the process and should be included in the mechanistic description.

Since the total amount of *exo* chloride (8) and bicyclo[3.3.1]non-2-ene-9-one (6) is nearly constant in all experiments, and 6 is easily derived from 8, then 9 seems to be formed to the expense of 7. In order to learn something more about the stability of the reaction products under cyclization conditions, compounds 6, 7, 8 and 9 were treated with AlCl_3 . The results which are summarized in Table 4 show clearly that all chlorinated cyclization products are interconvertible. *Endo* chloride (7) is found to have the lowest tendency to isomerize. 8 and 9 yield predominantly the elimination product 6. This low tendency to undergo structural change indicates, as

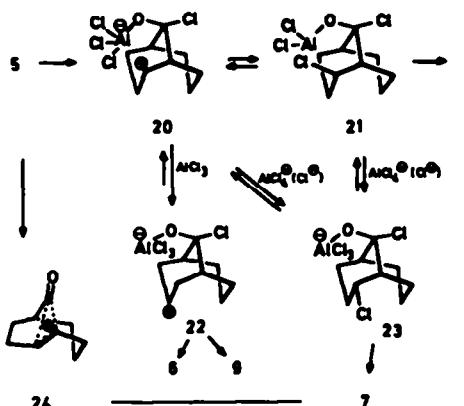
Table 4. Reaction of 6, 7, 8 and 9 with AlCl_3

Starting material	Time (h)	Reaction products ^b (%)	6	7	8	9	others
6 + HCl gas	6	54	—	9	37	—	
7	24	26	56	5	13	—	
8	24	64	2	11	23	—	
9	24	75	51	6	16	2-3	

^aReaction conditions: AlCl_3 , 1.1 mol in CCl_4 , 25° (Reflexing a reaction mixture of 6, 7, 8 and 9 with catalytic amounts of AlCl_3 in CCl_4 during two days did not alter the original ratio).

^bRatio detected by gic.

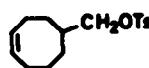
was discussed by Erman,^{4a} that 7 and 8 are primary cyclization products. In contrast 9 arises from a rearranged intermediate by intramolecular hydride shift. Since there must be a difference in the pathway for the first intermediate in the thermal and AlCl_3 -catalyzed cyclizations, we propose the following mechanism: In the thermal cyclization addition of the acid chloride function to the C=C double bond of 5 gives a "free" carbocation 19, which undergoes substitution to give 7 and 8 in a ratio reflecting their relative thermodynamic stabilities. 6 may arise either directly from 19 or by elimination of HCl from 8. The slightly favoured formation of *endo* isomer 7 over 8 could be rationalized in terms of nonclassical ion 24 and subsequent stereospecific attack by chloride ion.



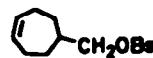
However, absence of any derivatives of bicyclo[4.2.1]nonane as well as the extensive hydride shift ($19 \rightarrow 9$) in the presence of AlCl_3 is hardly consistent with this conception. Although 7 seems to be very stable towards AlCl_3 , and to rearrange only to 9 up to 13%, the amount of 7 decreases from over 50% to nearly zero during the cyclization procedure within the 24 hr reaction time. This may reflect the fact that 24 is involved as an intermediate in the reaction to a greater extent than 13%. Disappearance of nearly all of 7 during the formation of 9 might be a consequence of the following: In the presence of molar amounts of AlCl_3 , the acid chloride 5 cyclizes to structure 20 bearing the aluminium moiety in the *syn* position because of the electrostatic attractive forces between the negative charge and the cationic center. From 20 the products 6, 7, 8 and 9 are formed through different intermediates 21, 22 and 23: transfer of chloride ion to C-2 gives *exo*-chloride 21; the intermediate 23 results from *endo* attack of AlCl_4^- ion to 20. Reversible transformation of 21 to 23, however, cannot be ruled out completely. In contrast to these kinetically controlled pathways the formation of 22 from 20 by hydride shift seems to be favoured during longer reaction times because of the higher thermodynamic stability of 22 compared to 21 and 23. The nearly complete disappearance of 7 during the 25 hr cyclization time, with the amount of 8 remaining almost constant, as well as the increasing formation of 9 in this reaction, may be due to the lower stability of intermediate 23 relative to 21. Intermediate 23 cannot be formed from 7 by reaction with AlCl_3 alone, and therefore it is understandable that 7 is less affected than 8 in this reaction (Table 4).

As anticipated above the cyclization of acid chloride 5 proceeds in a manner very similar to the solvolysis of

cyclooct-*cis*-4-ene-1-yl carbonyl tosylate 25. In fact previous investigations render it very unlikely that a nonclassical ion is involved in the cyclization of 25 as the sole intermediate because of the little stereoselectivity in product formation. The suggestion that classical ions must be involved also in the reaction of 25^{23,24} is now supported by the results which we obtained in cyclizing 5 or rearranging 7, 8 or 9.

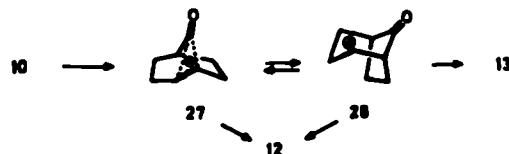


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A still more striking feature is to be found in the analogy between the cyclization behaviour of cyclohept-*cis*-4-ene-1-yl carbonyl brosylate (26)^{23,27} and cyclohept-4-*cis*-ene-1-carboxylic acid chloride (10). Both reactions gave predominantly the *endo* isomer (93%). This is consistent with a nonclassical ion 27 as proposed by Fickes and Kemp.³ The nearly quantitative stereoselectivity in product formation, and the absence of any hydride shift during the longer time (24 hr) AlCl_3 -reaction offer additional arguments for the involvement of 27. However, this ion cannot be the only reaction intermediate, because of a 7% formation of *exo* chloride 13 which can only be formed through classical ion 28.



EXPERIMENTAL

IR spectra were recorded on a Perkin Elmer Model 21. NMR spectra were obtained on a Varian A-60 A (60 MHz) and Bruker HFX 90 (90 MHz $^1\text{H-NMR}$ and 23 MHz $^{13}\text{C-NMR}$) spectrometers. All chemical shifts in CCl_4 (CDCl_3) solution are reported in parts per million (ppm) downfield from internal TMS. Mass spectra were recorded on a LKB 9000 Gas Chromatograph-Mass Spectrometer.

Column chromatography was carried out on silicagel 60 (Merck Darmstadt 70-230 mesh) using light petroleum (30-50)/ether mixtures as solvent with increasing proportions of ether. Normally product ratios were determined by glc analysis on a F & M. Model 810 gaschromatograph equipped with a 6 ft (1/8), packed column, 10% OV17 on Anachrom 90-100 A.S. All solvents used in this study were dried by passing them through Al_2O_3 , W 200 basic (M. Woelm, Eschwege) activity grade super 1.

Cyclooct-4-*cis*-ene-1-carboxylic acid chloride (5) was prepared by the method of Erman.^{4a}

Cyclohept-4-*cis*-ene-1-carboxylic acid chloride (10) was prepared in an analogous manner as 5 from cyclohept-4-*cis*-ene-1-carboxylic acid,²⁸ yield 82%, b.p. 77-79° (11 mm), NMR (CCl_4) δ 5.75 (2H, narrow m, C_4, C_5 , protons), 2.98 (1H, seven line m, C_1 , proton), 1.35-2.63 (8H, large m, $\text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$, protons). Acid amide m.p. 175-176°. Calcd. for $\text{C}_9\text{H}_{13}\text{NO}$: C, 69.03; H, 9.41; N, 10.06. Found: C, 69.58; H, 9.57; N, 9.41%.

Cyclization of acid chlorides without catalyst. Acid chloride (1-10 mmol) was refluxed in CCl_4 or dichloroethane (5-50 ml) until no more starting material was detectable in the NMR. After evaporation of the solvent the solid, slightly yellow (CCl_4) or brown ($\text{CHCl}_3-\text{CH}_2\text{Cl}$) product was purified by sublimation *in vacuo* (60-80°/12 mm). In the case of CCl_4 as the solvent, the products could be observed directly in the mixture by NMR

spectroscopy, after evaporation to an appropriate concentration. Yields and product ratios are summarized in Tables 1 and 2.

Cyclization of acid chlorides in presence of AlCl₃

General procedure. Acid chloride (10 mmol) in CCl₄ (2 ml) was added dropwise to a rapidly (magnetically) stirred slurry of anhydrous AlCl₃ (11 mmol) in 5–10 ml CCl₄.

All the time the flask was kept on the desired temp. and stirring was continued. After the reaction time (Tables 1 and 2) the complex was destroyed by adding 10–20 ml (5%) ice cold HCl, and the products isolated by ether extraction of the aqueous phase. The combined organic layers were washed successively with NaHCO₃, aq and brine, dried over MgSO₄, and the solvent was evaporated without heating.

Reaction products derived from 5 (Table 1). All compounds derived from 5 could be isolated pure to glc by column chromatography and preparative glc. Additionally considerable amounts of *exo* chloride (8) were separated from the mixture of isomers by fractional crystallization from petroleum ether (50/70). Compounds 6, 7 and 8 were identical with authentic samples.¹⁴ 3-Chlorobicyclo[3.3.1]nonane - 9 - one (9): (Calcd. for C₉H₁₄ClO: C, 62.61; H, 7.59; Cl, 20.53. Found: C, 62.58; H, 7.48; Cl, 20.58%). Colourless fine needles, m.p. 74–75°. IR (CCl₄) 1730 (strong) 1700 (medium, C=O) cm⁻¹. ¹H-NMR (CCl₄) 84.56–5.30 (1H, m, C₁ proton), 1.5–3.0 (m, large peak at 2.5–6H, C₁, C₂, C₃, C₄, C₅ protons and large peak at 2.12–6H, C₆, C₇, C₈, C₉ protons); ¹³C-NMR Table 3; mass spectrum (80 eV) m/e 67 (100), 172 (32), 174 (11).

HCl-Elimination from 9. 200 mg (1.16 mmol) of 9 were refluxed in 10% methanolic NaOH (10 ml) under N₂ for 12 hr. MeOH was evaporated without heating, the residue taken up with water (20 ml), the aqueous layer was extracted with four 20 ml portions of ether, the combined etheral phases washed with brine, dried (MgSO₄) and concentrated *in vacuo*. The volatile crystals (120 mg = 76% yield) obtained by this procedure were found to be identical to 6.

Reaction of 6, 7, 8 and 9 with AlCl₃. Chloroketone 7, 8 or 9 (1–2 mmol) were dissolved in 1 ml CCl₄ and added dropwise to a stirred slurry of AlCl₃ (1.1 mmol) in 2–4 ml CCl₄. After the desired reaction time, the mixture was worked up as it is described for the cyclization of acid chlorides in the presence of AlCl₃. In the case of 6, a slow stream of HCl gas was bubbled through the mixture. The results are summarized in Table 4.

Reaction products from 10 (Table 2). The ratio of 93% (12) and 7% 13 in the mixture induced some problems during the separation of both isomers. 12 can be isolated in about 50% by careful vacuum sublimation (25–30°/12 mm). The amount of the crude product of 13 in the residue is thus increased to about 20%. 13 can be obtained almost pure, contaminated by small amounts of 11 by treating the sublimation residue with 5% methanolic KOH (see below). 12 gave cyclohept - 4 - *cis* - ene - 1 - carboxylic acid in the reaction,¹ while after a 24 hr time only small quantities of 13 underwent elimination of HCl. Compound 13: (Calcd. for C₉H₁₄ClO: C, 60.37; H, 6.99; Cl, 22.35. Found: C, 60.41; H, 6.41; Cl, 21.95%), colourless crystals, purified by sublimation (70°/15 mm); m.p. 108–110°. IR (CCl₄) 1785 (weak) 1762 (strong) 1742 (shoulder C=O) cm⁻¹; NMR (CDCl₃) 4.48 (1H, m, half band width 9 Hz, C₁, *endo* proton); 1.5–2.6 (10H, structurated m, C₁, C₂, C₃, C₄, C₅, C₆, C₇, C₈, C₉ protons); mass spectrum (80 eV) m/e 95 (100), 158 (31), 160 (10). Compound 12:² Colourless soft crystals, m.p. 45–46°. IR (CCl₄) 1750 (C=O) cm⁻¹; ¹H-NMR (CDCl₃) 4.25 (1H, m, half band width 19.5 Hz, octet, J₁ = 3 Hz, J₂ = 6 Hz, J₃ = 10 Hz, C-2 *exo* proton); 2.56 (1H, m, J₁ = 5 Hz, J₂ = 1 Hz, C₁ proton); 1.4–2.45 (9H, m, C₁, C₂, C₃, C₄, C₅, C₆, C₇, C₈, C₉ protons); mass spectrum (80 eV) m/e 95 (100), 158 (18), 160 (6).

Treatment of 12 and 13 with 5% methanolic KOH. The mixture of 10 (1.5 g 9.4 mmol) was dissolved in 70 ml 5% methanolic KOH aq and refluxed for 24 hr. The soin was cooled, and most of the MeOH evaporated without heating. The residue was taken up in water (100 ml) and extracted 4 times with ether. The combined etheral layers were washed with brine, dried (MgSO₄) and the solvent evaporated to yield 120 mg of 13, which contained various amounts (5–10%) of 10. The aqueous layer was neutralized by adding diluted HCl, and extracted several times with ether, the etheral phases washed with brine, dried (MgSO₄)

and the solvent evaporated to afford 1.1 g of cyclohept - 4 - *cis* - ene - 1 - carboxylic acid, m.p. 70–71% (50% EtOH) (Ref. 28 75.5%).

Reaction of *exo* and *endo* 2-hydroxybicyclo[3.3.1]nonane - 9 - one (14) and 2-hydroxybicyclo[3.2.1]octane - 8 - one (16) with POCl₃. 22 ml of POCl₃ was added dropwise to a stirred, ice cooled mixture of the alcohol (10 mmol) in 75 ml of dry pyridine. After one day at room temp. the soin was worked up by very slow addition of water (caution!) until no more POCl₃ was present. The aqueous layer was extracted four times with ether, the etheral phases neutralized with NaHCO₃, aq, washed with brine, and the solvent evaporated. The remaining mixture was separated by column chromatography. The compounds isolated proved to be identical with 7 and 8 in the bicyclononane series and with 12 and 13 in the case of bicyclooctane derivatives, in all spectroscopic and chemical properties. As a function of temp. variable amounts of the unsaturated ketones 6 and 11 were found in the mixtures.

Bicyclo[3.2.1]oct-2-ene-8-one (11). 4.2 g benzoylchloride (33 mmol) were added to 3 g (21.4 mmol) of 16 in 4 ml pyridine and the mixture was heated to 120° for 1 hr. After standing for 2 hr at room temp., the mixture was quenched with ice (50–70 g) and extracted with four 50 ml portions of ether. The combined etheral extracts were washed with NaHCO₃, aq and brine, dried (MgSO₄) and the solvent evaporated. The remaining crude benzoate (6 g, 82% yield) was heated in a distillation apparatus with a free flame to effect slow distillation at 240–290°. The product, that remained mainly in the condenser, was taken up in ether, the etheral soin washed with diluted NaOH aq and brine, dried (MgSO₄) and concentrated *in vacuo*. The liquid residue (1.9 g), which was nearly pure to glc was distilled to yield 1 g (33%) of 11, b.p. 72–73° (12 mm) (Ref. 22a 130°/25 mm). 11 darkened on standing and was obviously partially decomposed during distillation.

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REFERENCES

- J. K. Groves, *Chem. Soc. Rev.* 1, 73 (1972).
- M. A. McKervey, D. Faulkner and H. Hamill, *Tetrahedron Letters* 1971 (1970).
- G. N. Fickes and K. C. Kemp, *Chem. Commun.* 84 (1973).
- W. F. Erman and H. C. Kretschmar, *J. Org. Chem.* 33, 1545 (1968); E. N. Marvell, R. S. Knutson, T. McEwen, D. Sturmer, W. Federici and K. Salisbury, *Ibid.* 35, 391 (1970).
- S. A. Monti and G. L. White, *Ibid.* 40, 215 (1975).
- A double cyclization reaction yielding spiro compounds has been described by M. F. Semenoff, J. S. Foo and S. Katz, *J. Am. Chem. Soc.* 95, 7325 (1973).
- S. Moon and T. F. Kolesar, *J. Org. Chem.* 39, 995 (1974).
- G. L. Buchanan, in *Topics in Carbocyclic Chemistry* (Edited by D. Lloyd), Vol. 1, p. 199. Logos Press, London (1969).
- W. Kraus, W. Rothenwöhler and R. Chassan, *Tetrahedron Letters* 4581 (1969).
- W. Kraus, G. Klein, H. Sadlo and W. Rothenwöhler, *Synthesis* 485 (1972); W. Kraus, W. Rothenwöhler, H. Sadlo and G. Klein, *Angew. Chem.* 84, 643 (1972), *Ibid. Internat. Edit.* 11, 641 (1973).
- W. Kraus and W. Rothenwöhler, *Tetrahedron Letters* 1007, and 1013 (1968).
- P. G. Gassman and J. L. Marshall, *J. Am. Chem. Soc.* 88, 282 (1966); P. G. Gassman, J. L. Marshall, J. G. Macmillan and J. M. Hornback, *Ibid.* 91, 4282 (1969).
- M. Hanack and J. Dolde, *Tetrahedron Letters* 321 (1966).
- When this study was nearly completed Fickes and Kemp (Ref. 3) reported the stereoselective cyclization of 10 to give 100% of 11 in presence of molar amounts of AlCl₃. This observation deviates slightly from our own results.
- R. D. Allan, B. G. Cordiner and R. J. Wells, *Tetrahedron Letters* 6055 (1968).
- In the case of compounds 7 and 8 all nine ¹³C-resonance lines have been determined: A. Heumann and H. Kolbhorn, *Tetrahedron* 31, 1571 (1975).

¹⁷N. C. Webb and M. R. Becker, *J. Chem. Soc. (B)*, 1371 (1967).

¹⁸W. D. K. Macrae, J. Martin and W. Parker, *Tetrahedron Letters* 2589 (1965).

¹⁹cf.: M. Fisch, S. Smallcombe, J. C. Gramain, M. A. McKervey and J. E. Anderson, *J. Org. Chem.* 35, 1886 (1970).

²⁰J. B. Stothers, *Carbon-13 NMR Spectroscopy*, Academic Press, New York (1972); ²¹N. K. Wilson and J. B. Stothers, In *Topics in Stereochemistry* (edited by N. L. Allinger and E. Eliel), Vol. 8, Wiley, New York (1974).

²¹*endo* 3-Substituted bicyclo[3.3.1]octanes show a marked high field shift (6.3 ppm) for C₁ in comparison to the corresponding hydrocarbon, while *exo* isomers differ only by 0.1 ppm from the hydrocarbon: H. Kolshorn and A. Heumann, submitted for publication; cf. J. R. Wiseman and H. O. Krabbenhoft, *J. Org. Chem.* 40, 3222 (1975).

²²cf.: C. S. Foote and R. B. Woodward, *Tetrahedron* 20, 687 (1964); ²³N. A. LeBel and L. A. Spurlock, *Ibid.* 20, 215 (1964); ²⁴11 was synthesized independently by pyrolyzing the benzoate of alcohol 16; cf: R. D. Allan and R. J. Wells, *Austral. J. Chem.* 23, 1625 (1970).

²⁵The enormous difference in reaction time between CCl₄ and 1,2-dichloroethane as a solvent is not yet understood. The dissociation of C₂H₅Cl₂ (CH₂Cl-CH₂Cl \rightleftharpoons CHCl-CH₂...HCl) might liberate HCl, which may react as a Lewis acid and catalyze the cyclization. This is not possible in CCl₄, so that only a simple thermal reaction takes place.

²⁶Hydride shifts during AlCl₃-catalyzed acylation of double bonds have been described. They lead to ketocarbenium ions, where the positive charge is located on the carbon furthest from the CO group.⁴⁴

²⁷H. Felkin, G. LeNy, C. Lion, W. D. K. Macrae, J. Martin and W. Parker, *Tetrahedron Letters* 157 (1966); ²⁸C. Chuit, H. Felkin, G. LeNy, C. Lion and L. Prunier, *Tetrahedron* 28, 4787 (1972).

²⁹M. Hanack, W. Kraus, W. Rothenwöhrer, W. Kaiser and G. Wentrup, *Liebigs Ann.* 703, 44 (1967); and refs cited.

³⁰G. LeNy, C. R. hebdo. Séanc. Acad. Sci. 251, 1526 (1960).

³¹G. Stork and H. K. Landesmann, *J. Am. Chem. Soc.* 78, 5129 (1956).