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REARRANGEMENT AND CYCLIZATION IN THE IONIZATION OF THE 4-CHLORO-3-METHYLBUTANOYL CATION

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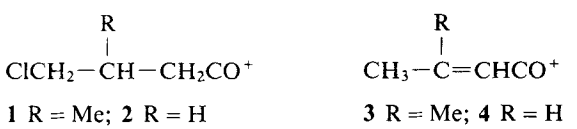
The second ionization of the 4-chloro-3-methylbutanoyl ion forms a primary alkyl acyl dication, as a tight ion pair. Methyl and hydrogen shifts occur to comparable extents indicating that the relative stability of the product (*sec*- or *tert*-carbocation) does not influence the energy barrier for the shift. The product of methyl shift (1,3-*sec*-alkyl acyl dication) loses the proton closest to the counterion in the tight ion pair and forms the pent-3-enoyl cation. Protonation–deprotonation of the latter, followed by internal acylation, gives the protonated cyclopent-2-enone. The dication resulting from hydrogen shift loses a proton from C-2 and gives the 3-methylbut-2-enoyl cation.

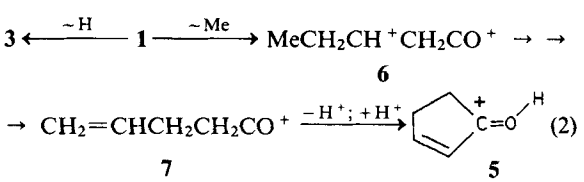
INTRODUCTION

As part of our studies on acyl alkly dications,[1] we have investigated the reaction of the 4-chloro-3-methylbutanoyl cation (**1**) in superacids. Based on our findings with the lower homolog, the 4-chlorobutanoyl cation (**2**),[1] we expected **1** to form the 3-methylbutenoyl cation (**3**) in an acidity-dependent reaction [equation (1)]. We reasoned that a concerted hydride shift might assist ionization of **1**, such that the latter would not show the mechanistic complications observed in the coversion of **2** to **4**, and it would react at lower acidities, thus expanding the range for which conversion rates of chloroacyl cations could be used as acidity probes.[2,3]



1 R = Me; **2** R = H **3** R = Me; **4** R = H (1)

Cation **1** was generated from the acid chloride, the synthesis of which is detailed under Experimental. The reaction of **1** was studied in three superacids: (A) FSO_3H–SbF_5 (4:1) (B) FSO_3H–SbF_5 (1:1) and (C) HF–SbF_5 (1:1). On standing, the ^1H NMR spectrum of **1** (δ1·48, d, 3H; 3·23, m, 1H; 3·85, m, 2H; 4·13, m, 2H)[4] was replaced with that of **3** (δ2·78, s, 3H; 2·86, s, 3H; 6·50, s, 1H)[5] and of protonated cyclopent-2-enone, **5** (δ3·40, s, 4H; 7·09, d, 1H; 9·28, d, 1H).[6] The reaction therefore involves a competition between a hydrogen and a methyl shift, after ionization or concerted with it [equation (2)]. In each instance the migration increases the charge repulsion, as a 1,3-dication is formed from a 1,4-dication, but at the same time it converts a primary carbocation to a tertiary and to a secondary carbocation, respectively.



(2)

An analogy to the formation of **5** exists in the reaction of 1,3-dimethylallyl cation with carbon monoxide. The β,γ-unsaturated acyl cation first formed in that reaction undergoes double-bond migration and cycloacylation giving the protonated 2-methylcyclopent-2-eone.[7]

The conversion was clean in acids A and B, and rates could be measured; some side products formed in acid C prevented an accurate kinetic study. The rate of disappearance of **1** increases with increasing acid strength. Thus, about 50% conversion to products occurred in 250 min in acid A at 53·5 °C, in 40 min in acid B at 54·0 °C and in less than 100 min in acid C at 23·8 °C (the side reactions were prevalent in acid C at higher temperatures). For comparison, the parent ion **2** is about half converted to **4** in 250 min in acid A at 53·8 °C and in 85 min in acid C at 28 °.[1] The near equality in rates between **1** and **2** would seem to argue against assistance of ionization of **1** by the methyl and

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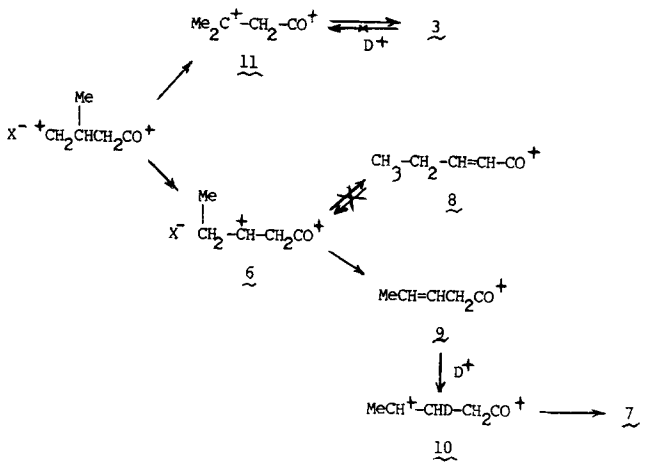
hydrogen shifts, but the comparison is not straightforward, because mechanistic differences were evidenced. Thus, an intermediate was observed for the reaction of **1** in both acids A and B; it exhibited a doublet at δ 1·79, which could be integrated. The conversion of **1** to the intermediate exhibits first-order kinetics ($k_1 = 4{\cdot}97 \times 10^{-5}\ s^{-1}$ at 53·5 °C in acid A and $1{\cdot}71 \times 10^{-4}\ s^{-1}$ at 54·0 °C in acid B) and shows no induction period.

The ratio of **3** to **5** remains constant throughout reaction in acids A and B. In addition, the rates of formation of the two products depend on the intermediate concentration in a similar way, thus indicating that the intermediate is common to the two pathways, and therefore has an unrearranged structure. It is probably the analog of **1** with Cl replaced by fluorosulfate. Similar replacements of substrate leaving group by the superacid anion have been reported before.[6] Acid catalysis in the formation of the intermediate (faster reaction in acid B) indicates capture of a primary alkyl acyl dication, rather than nucleophilic displacement of chloride in **1**.

The relative importance of the two pathways depends on both acidity and temperature. Thus, the ratio: **3**:**5** is 1·46 in acid A at 53·5 °C and 0·69 in acid B at 54·0 °C. The ratio in acid A is 1·28 at 57·8 °C and 2·79 at −19 °C. In acid C the ratio changes with conversion (>1 initially, <1 at more than 50% conversion). Again, the sizeable extent of side reactions prevented a careful study in acid C, but a control experiment showed no conversion of **3** to **5**. The similar amounts of **3** and **5** observed indicate that the stability of the migration products (tertiary cation for the formation of **3**, secondary cation for the formation of **5**) plays no significant role in determining which group migrates.

A difference between the two pathways appeared in the reaction of **1** in deuterated acid B. Deuterium NMR shows one strong peak at 3·40 ppm (C-4 or C-5 of **5**, or both), and very small incorporation in other positions of **5**, or in **3**. ^{13}C NMR[8] confirmed this finding. The isotope exchange can result from the deuteration[9] of an alkenoyl cation intermediate in the formation of **5**, which indicates that the 1,3-dication, **6**, resulting from a methyl migration reacts further by proton loss rather than a hydride shift. Of the two possible elimination products, the α,β-unsaturated structure (pent-2-enoyl cation, **8**) would lead to incorporation of deuterium at C-5 in the cyclic product. This pathway is unlikely, however, because the branched α,β-alkenoyl cation **3** formed in the reaction, which should be protonated more easily than **8**, incorporates no deuterium. It remains that proton elimination to form the less stable β,γ-unsaturated alkenoyl cation isomer, **9**, is the preferred reaction of **8**. As shown in Scheme 1, conversion of **9** to **7** through dication **10** places a deuterium atom at C-3, which becomes C-4 of the cyclic product, **5**, Formation of the 1,4-dication **10** from **9** is obviously preferred to the formation of the 1,3-dication **6**.

The proton loss that occurs in the formation of **9** cannot be concerted with the methyl migration and assist it kinetically (base catalysis[1]), because the ratio **5**:**3** is higher in the stronger acid B than in acid A. The results are best rationalized by a competitive migration in the primary alkyl acyl dication (1,4-dication) followed by proton loss from the 1,3-dication (**6** or **11**, Scheme 1). The secondary ion **6** transfers the proton closest to the counter ion serving as the base, in the tight ion pair, and gives the pent-3-enoyl cation (**9**), while **11** survives long enough to allow the base to remove the proton at C-2 and form **3**.



Scheme 1

EXPERIMENTAL

General procedures. The gas chromatograms were run on a 3 m × 3 mm o.d. column with 10% silicone SP-1000 on Supelcoport as stationary phase. The ^{1}H NMR spectra of neutral species were recorded at 60 MHz and their ^{13}C NMR spectra were obtained at 62·896 MHz, all in $CDCl_3$ with TMS as internal standard. The conversion of ion **1** was followed by ^{1}H NMR at 90 MHz; the chemical shifts were measured from external (coaxial) TMS dissolved in $CDCl_3$.

4-Chloro-3-methylbutanenitrile (**12**). A warm solution of NaCN (21·4 g) in water (33 ml) was diluted with 95% ethanol (130 ml), then 1-bromo-3-chloro-2-methylpropane (62·2 g) was added dropwise and the mixture was boiled under reflux until the ratio of product to starting material was 6–9 [by gas–liquid chromatography (GLC)]; about 3·5 h were necessary. Very little of a material with a longer retention time (presumably the dinitrile) was observed. The reaction mixture was diluted with 150 ml of water and extracted with 4 × 25 ml of methylene chloride. The combined organic solution was washed with a solution of 50 g of calcium chloride hexahydrate in 37 ml of water, then with distilled water (90 ml) and dried over $CaCl_2$. The solvent was evaporated and the product was distilled on a 15 cm long annular column at 12 Torr (1 Torr = 133·3 Pa). A small amount of unreacted starting material (5·6 g, b.p. 47–48 °C) and a mixture of the latter with the product (2·3 g) were first collected, then the product (**12**, 29·7–30 g, 69·5–70% yield) distilled at 83–84 °C/11–12 Torr. Its purity was 98·5% (GLC). The yield was nearly double that reported for a lower conversion of the starting material.[10]

IR: 2212 cm (C≡N). ^{1}H NMR: 1·16 (d, 3H), 1·9–2·7 (complex, 3H), 3·2–3·7 (complex, 2H). ^{13}C NMR: 17·31, 21·73, 32·00, 48·52 (CH_2Cl), 117·99 (CN).

Hydrolysis of **12**. The nitrile (14·25 g) was added to 36% hydrochloric acid (19 ml) and boiled under reflux[11] for 18 h. Water (18 ml) was added, and the mixture was extracted with three 25-ml portions of diethyl ether. Drying (Na_2SO_4) and evaporation of the solvent left a mixture of 4-chloro-3-methylbutanoic acid (**13**) and 3-methyl-γ-butyrolactone (**14**) in comparable amounts (8·0 g, *ca* 50% yield). Attempts to isolate pure **13** by extraction with cold 10% aqueous sodium hydrogen-carbonate solution, followed by careful acidification and diethyl ether extraction, gave a product that still contained some lactone, which is readily soluble in both water and diethyl ether.

13: ^{13}C NMR 17·79 (CH_3), 32·32, 38·01, 49·92 (CH_2Cl), 177·68 (COOH).

14: ^{13}C NMR, 17·93 (CH_3), 30·42 (CH), 36·15 (CH_2), 74·72 (CH_2), 177·29 (COOR).

4-Chloro-3-methylbutanoyl chloride (**15**). Sodium hydroxide (7·5 g) was dissolved in methanol (75 ml), a *ca* 1:1 mixture of **13** and **14** (22·5 g, about 0·191 mol) was added, then 2 drops of alcoholic phenolphthalein, and the solution was stirred until all the base was consumed (overnight). A further 0·5 g of sodium hydroxide was added, the solution was stirred for 2 h and the solvent was distilled off under vacuum. The resulting cake, still wet, was broken in to small lumps with a spatula, then evaporation was continued until the solid no longer looked wet. The material was ground in a mortar, then dried for 1 day at 100 °C and 4 Torr.

The sodium salt was added in small portions to thionyl chloride (95 ml) maintained at −50 °C and stirred magnetically. The suspension was allowed to warm to room temperature overnight, and finally boiled under reflux for 2 h. After cooling, the mixture was filterred with suction through a sintered-glass funnel, the excess of thionyl chloride was distilled off at atmospheric pressure and the residual oil was fractionated under vacuum on a 15 cm long annual column. Pure **15** (9·35 g, 27–32% yield) distilled at 73–5 °/12 Torr. A fraction containing some lactone **14** (4·54 g, 13·1–15·4% yield) was collected at 76–78 °C/12 Torr.

15: ^{1}H NMR, 3·46 (2H, distorted d), 3·2–1·8 (3H, m), 1·08 (3H, d); ^{13}C NMR, 17·36 (CH_3), 32·80 (CH), 49·01 (CH_2), 50·80 (CH_2), 172·61 (COCl).

Acyl cation **1**. Acid chloride **15** was added to the superacids directly in the NMR tubes, under nitrogen in a dry-box, at −78 °C. The tubes were then sealed on a vacuum line, and placed in a thermostated bath (or in the variable-temperature probe of the NMR instrument) maintained at the desired temperature. The conversion of **1** was followed by ^{1}H NMR.

1: ^{1}H NMR, 1·48 (d, 3H), 3·23 (m, 1H), 3·85 (m, 2H), 4·13 (m, 2H).

5: ^{1}H NMR, 3·40 (s, 4H), 7·09 (d, 1H), 9·28 (d, 1H).

3: ^{1}H NMR, 2·78 (s, 3H), 2·86 (s, 3H), 6·50 (s, 1H).

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