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1,3- AND 1,5-MIGRATIONS INVOLVING CHLORINE

LÁSZLÓ TŐKE*, ZOLTÁN BENDE, ISTVÁN BITTER, GÁBOR TÓTH, PÁL SIMON[a]
AND RUDOLF SOÓS[b]

Department of Organic Chemical Technology, Technical University,
H-1521 Budapest, [a]Central Research Institute for Chemistry of
Hungarian Academy of Sciences, H-1525 Budapest, [b]Chinoin
Pharmaceutical and Chemical Works Ltd. H-178o Budapest, Hungary

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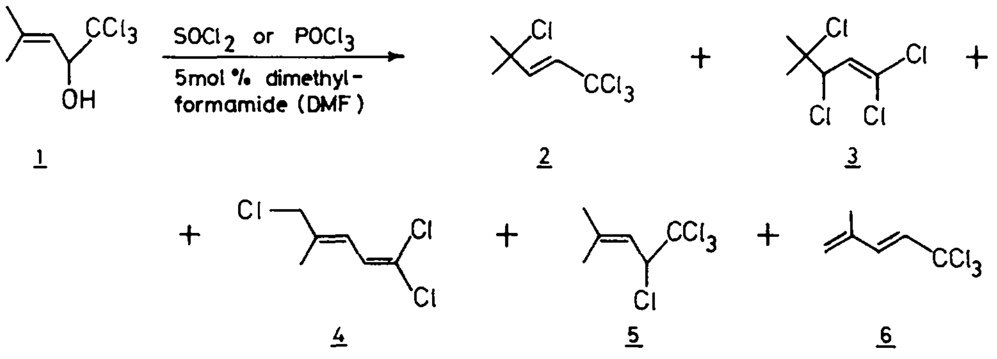
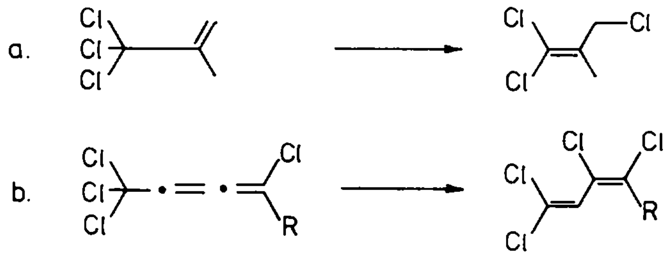
Abstract - Rearrangement processes involving chlorine have been observed in the reaction of 1,1,1-trichloro-2-hydroxy-4-methyl-pentene-3(1) with inorganic acid chlorides. Conversion of compound 2 to 3 represent a new example of a 1,3-chlorine shift. Formation of compound 4 from 6 is a new type of rearrangement involving 1,5-chlorine migration, and at the same time, is a good example of the role of kinetic vs. thermodinamic control in chemical processes. The transformations were found to proceed via radical intermediates.

We have investigated the replacement of the hydroxyl group by chlorine in 1,1,1-trichloro-2-hydroxy-4-methyl-pentene-3 (1). A number of different chlorinated compounds were formed[1], and of these, the trichloro-methyl substituted alkenes showed interesting rearrangement phenomena.



Scheme 1.

Rearrangement reactions of allyl halides are described in the literature[2-5] and are of considerable practical importance. Yet, with the exception of the isomerizations during solvolysis of allyl chlorides, the detailed mechanisms of these reactions have received little attention[4]. This is also the case for rearrangement of trichloromethyl-substituted alkenes, eg.for the rearrangement of 1,1,1-trichloro-2-methyl-2-propene to 1,1,3-trichloro-2-methyl-1-propene catalysed by thionyl chloride, softglass or ketene diethyl acetal (Scheme 2,a). It was proposed[2,3] that the electron-donor character of these catalysts is responsible for catalysis of the isomerization. In another case (Scheme 2,b) a 1,3-shift exerted by sand was recognized but mechanistic details were again missing.[5]



Scheme 2.

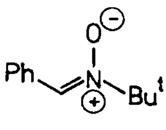
We report here an additional example of the 1,3-chlorine rearrangement and a new type of rearrangement involving 1,5-chlorine migration. Efforts to elucidate the mechamism of these processes are also presented.

RESULTS AND DISCUSSION

In the previous publication[1] we described the preparation of the compounds 2,3,4,5 and 6 by the reaction of alcohol 1 with inorganic acid chlorides (Scheme 1). The three main components of the product mixture compounds 2, 3 and 4 were separated on preparative scale, but being very sensitive towards heat, compound 6 could be isolated only as a mixture of 6 (70 %) and 2 (30 %), while the presence of 5 ($\sim$1 %) was substantiated by GC-MS experiments[6]. During the procedures of the separation and purification transformations involving rearrangements 2 to 3 and 6 to 4 were observed by GLC. In order to further investigate these processes, the experiments were carried out in NMR and ESR tubes and the changes were monitored by the appropriate spectroscopic method.

1,3-Rearrangement of compound 2 to 3

After 6 hours heating at 130-140 °C, compound 2 rearranged completely to 3 as the sole product (see Experimental). The transformation was irreversible because starting from pure 3 no sign of the formation of 2 was detected. The process was found to be dependent on the time and the temperature; taking 2 hours for 10 % conversion at 140°C, while below 80°C no transformation could be observed. The presence of any radical species in the allylic rearrangement process 2 → 3 could not be detected either by the CDNP method or by ESR in the temperature range (60-140°C) used. However, the application of N-t-butyl-α-phenylnitrone (7) as spin trap[7] made possible the ESR investigation of the process. In the spectra recorded at the transformation 2 → 3, in the presence of 30 mol % nitrone 7 and in the temperature range 90-140°C, intense lines were appearing with coupling constants a_N=14.65 G and a_H=2.48 G showing the formation of a spin adduct[8] of the possible structure 8. It was also shown that the appearance of the radical species was strictly connected with the rearrangement process 2 to 3, because no radical was detected in a mixture of 3 with nitrone 7 under the above mentioned conditions. NMR investigations, however, showed that in the presence of nitrone, beside compound 3, compound 4 was also formed in a ratio depending on the quantity of the nitrone used. A possible explanation for formation of 4 in these conditions is the decomposition of the spin adduct 8 and the subsequent recombination of the radicals formed (Scheme 3).



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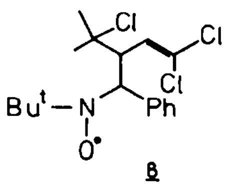

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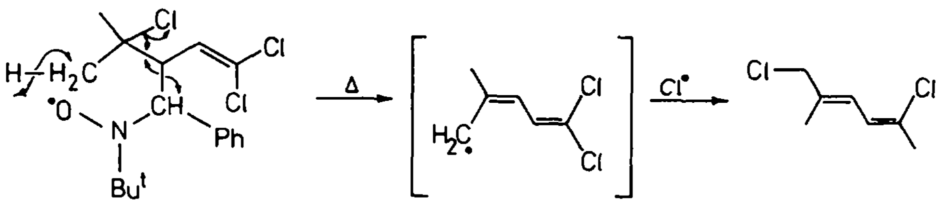

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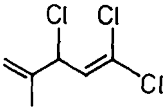
Scheme 3.

1,5 Rearrangement of compound 6 to 4

Transformation of compound 6 to 4 was studied with a mixture of compound 6 and 2. The complete conversion of 6 to 4 took about 8 hours at 7o-75 ^{o}C. The rearrangement was observed to proceed at ambient temperature, too. At the same time we proved by NMR that rearrangement of 2 to 3 could be excluded in these conditions. Transformation of 6 to 4 was also irreversible because pure 4 remained unchanged by heating. From mechanistic point of view it was very important observation that during the transformation not only the signals of the endproduct 4 could be seen but also those of an other product for which structure 9 was assigned on the basis of the ^{1}H NMR data. It could be observed however, that after 2 hours at 7o-75^{o}C, the percentage numbers for 4 and 9 were 15-2o % and 5-1o %, after 5 hours 4o % and less then 1o %, respectively. By the end of the reaction practically complete transformations of 6 and 9 to 4 were detected (see Experimental). Transformation of 6 to 9 and to 4 in parallel processes is a new example to show the role of the kinetic versus thermodinamic control in chemical processes. At the beginning of the reaction the ratio of compounds 9 to 4 is controlled by kinetic parameters; the rate constant for 1,3-chlorine shift leading to 9 was comparable to that of the 1,5-chlorine shift affording 4 but, being the process of the formation of 9 reversible, its proportion was continuously decreased transforming itself to the thermodinamically more stable 4. For a sufficiently long period of time the result was determined by the stability relationships of the products (Scheme 4).



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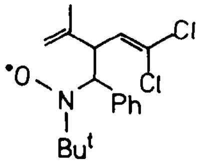
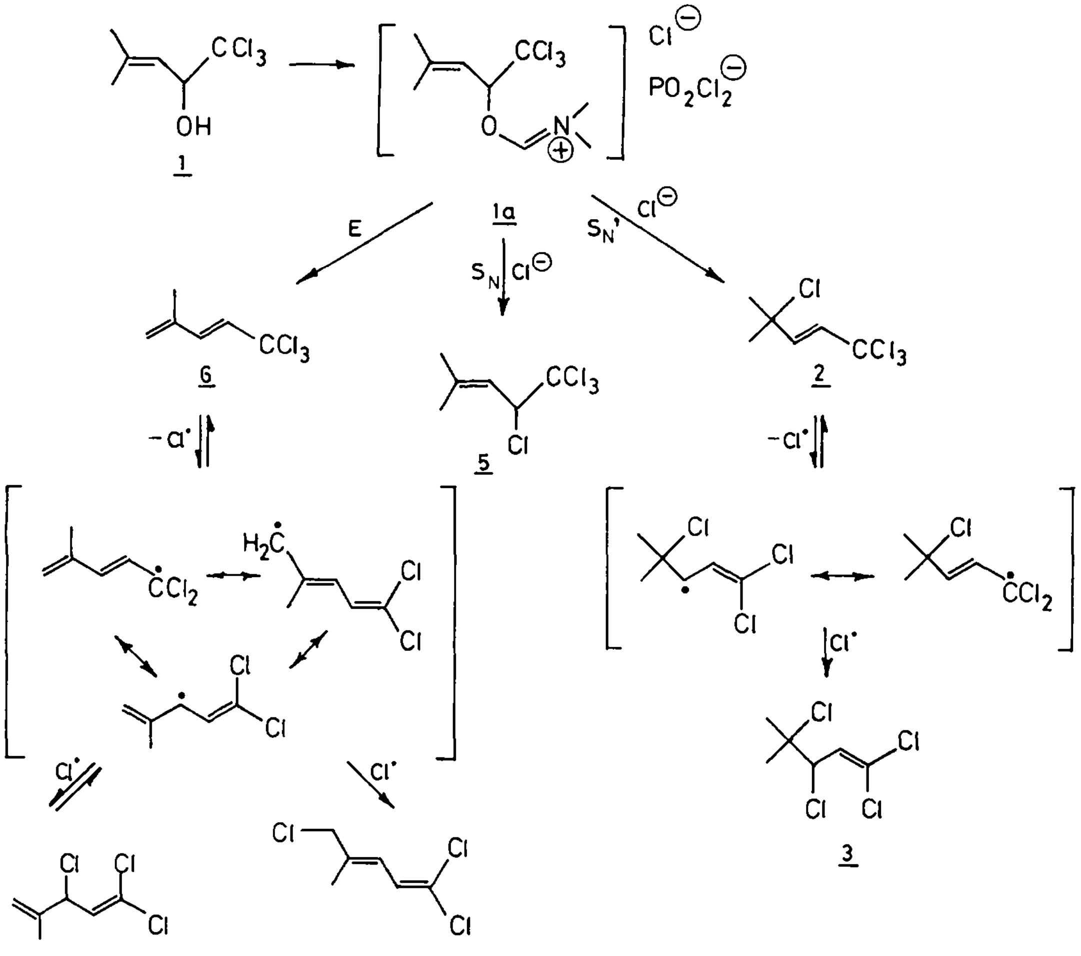
Radical character of these processes could only be seen again if nitrone 7 was added to the reaction mixture. The coupling constants a_N = 15.o3 G, a_H = 5.56 G in the ESR spectra indicated the formation of spin adduct^{9,1o} with possible structure 1o. The direction of the transformations did not change when nitrone 7 was used but, surprisingly, the rate of the rearrangements was increased (see Experimental). This phenomenon may due to the inhibition of the reaction $6 \rightleftarrows 9$ by reversible formation of the adduct 1o. Reaction $6 \rightleftarrows 9$ can be considered as a "side reaction" on the way of the overall transformation process $6 \longrightarrow 4$, and consequently, the inhibition of the "side process" increases the concentration of 6 in the reaction mixture.



1o

To summarize all these observations we propose the mechanism shown in Scheme 4 for the reaction of 1 with inorganic acid chlorides. The intermediate 1a reacts in three different routes. S_N' and S_N processes result in the formation of 2 and 5, respectively. Proton and DMF elimination, on the other hand, affords compound 6. The ratio of substitution to elimination depends on the nature of the anion



Scheme 4.

in the intermediate 1a. If it is chloride anion (when $SOCl_2$ is used in the reaction) the substitution is the main process with the formation of a product mixture containing 2+3 and 4 in a ratio of about 8o:2o. When using $POCl_3$, the appropriate dichlorophosphate anion acts as a more powerful proton abstracting agent and so the formation of 6 and its subsequent rearrangement to 4 is preferred. This explanation is supported by the observation that addition of solubilized chloride ion (triethyl-benzyl-ammoniumchloride) to the mixture of 1 with $POCl_3$ helps the substitution resulting in a product ratio of 2+3 to 4 (25:75), considerably higher than that (5:95) found in the absence of added salt (see the previous paper[1]).

EXPERIMENTAL

The reactions were monitored by GLC using a HP 575o chromatograph with an analytical column (2m, 3 % QF1 on Chromosorb W), at 13o °C. Samples were diluted to about 5 vol % before injection. Evaporation temperature was not to exceed 17o-175 °C. The consumption of 1 in the chlorinations was detected by TLC (POLYGRAM SIL G, benzene:methanol=1o:1, phosphorus molybdenic acid in ethanol, R_f(1):o.53, R_f(all chlorinated products):o.69). The ^1H NMR spectra were recorded in $CDCl_3$, in the PFT mode (16 K data points for the FID) at 99.6 MHz with internal deuterium lock, using a JEOL FX-1oo multinuclear spectrometer. The chemical shifts were determined on the δ scale with tetramethyl silane as internal standard. (For the IR, ^{13}C NMR, MS and complete ^1H NMR spectra see the previous paper[1]). ESR spectra were detected by a JEOL-FE-3X spectrometer at 1oo KHz modulation frequency. The temperature was varied by a JES-VT-3AZ variable temperature controller with an accuracy of ±1 °C.

NMR Investigations of the rearrangements

Transformation of 2 to 3. 66.6 mg (o.3 mmol) neat 2 and (in parallel experiments) mixtures of 2 with 5o or loo mol% N-t-butyl-α-phenyl nitrone (7) were heated at 14o±3°C for 2-6 hours. The products were dissolved in o.6 cm^3 $CDCl_3$ and the ^1H NMR spectra were recorded at ambient temperature. The product ratios for 2 to 3 and to 4 were estimated according to the relative intensities of signals 6.27d, 6.43d (14.6 Hz); 4.7od, 6.12d (9.5 Hz) and 4.o3s, respectively.

Table 1. Rearrangement of 2 to 3

Nitrone (7) (mg)	(mol%)	Time (h)	Composition (mol%) 2	3	4
29.6	5o	2	85	5	lo
-	-	2	9o	lo	-
59.1	loo	6	5	5o	4o[a]
-	-	6	<5	9o	-[a]

[a] 5-lo mol% unidentified products

Table 2. Rearrangement of 6 to 4

Nitrone (7) (mg)	(mol%)	Time (h)	Composition (mol%) 2	6	9	4
-	-	2	3o	45	5-lo	15-2o
-	-	3.5	3o	4o	lo	2o
-	-	5	3o	2o	lo	4o
-	-	8	3o	<3	<3	>65
28.3	o.16	2	3o	4o	lo	2o
56.6	o.32	3.5	3o	<5	~lo	6o
28.3	o.16	5	3o	<5	<5	>65

Transformation of 6 to 4. 9o mg mixtures of 7o mol% (~ o.32 mmol) 6 and 3o mol% 2 with or without nitrone 7 were dissolved in o.6 cm^3 $CDCl_3$. The solutions were transferred into NMR tubes and were heated at 75±3°C for 2-8 hours, then ^1H NMR spectra were recorded at ambient temperature, the ratios for 2:4:6 and 9 were estimated on the basis of signals 6.27d, 6.43d (14.6 Hz); 6.55d (1o Hz), 4.o3s; 6.71d (15 Hz), 5.21s and 4.95s, respectively.

^1H NMR spectrum of 1,1,3,-Trichloro-4-methyl-1,4-pentadiene (9)

(Determined from the reaction mixture): 1.73-1.87 (CH_3; in overlap with the methyl signals of 2,4 and 6), 4.95(s, 2 H_2C=), 5.16(d,1 J=lo Hz, CHCl) 6.12(d,1 J=lo Hz, $CH=CCl_2$).

E.S.R.investigations of the rearrangements

Transformation of 2 to 3. A sample of 4o mg (o.18 mmol) 2 and lo mg (o.o56 mmol) nitrone (7) was heated to 14o°C for 2o minutes and then detected at ambient temperature. a_N=14.65 G a_H=2.48 G.

Transformation of 6 to 4. 28 mg mixture of 7o mol% 6 (~ o.1 mmol) and 3o mol% 2 and 3.6 mg (o.o2 mmol) nitrone (7) was kept at 36 °C and simultaneously detected, thus avoiding the rearrangement of 2. a_N=15.o3 G, a_N=5.56 G.

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