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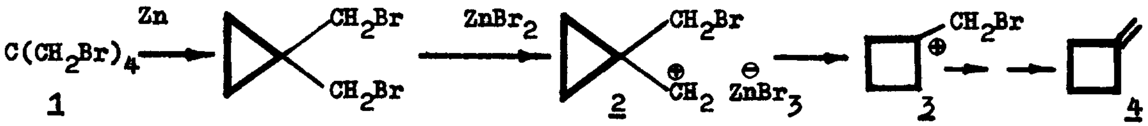
MECHANISM OF THE GUSTAVSON REARRANGEMENT. REACTION OF TETRAHALONEOPENTANES, ESTERS OF TRIBROMONEOPENTANOL AND THEIR CYCLOPROPYL ANALOGS WITH ZINC.

A.I.Dyachenko*, E.L.Protasova, A.I.Ioffe, A.Ya.Steinschneider and O.M.Nefedov*
N.D.Zelinsky Institute of Organic Chemistry, USSR Academy of Sciences,
Moscow, USSR

The formation of methylenecyclobutane in the reaction of tetrahaloneopentanes and related compounds with zinc is shown to proceed via organozinc intermediates.

The Gustavson rearrangement, i.e. the formation of methylenecyclobutane in the reaction of tetrabromoneopentane with zinc in aqueous ethanol, is traditionally believed to proceed via a carbonium ion mechanism due to C-Br bond ionisation by $ZnBr_2$, formed in the course of dehalogenation[1]:



The arguments in favour of this mechanism are the formation in this reaction of the by-product 2-methyl-1-butene (according to ref. 2 the corresponding open-chain carbonium ion can equilibrate with 2 and 3) as well as the total inhibition of the rearrangement when Zn^{++} ions are excluded[3].

At the same time the possibility for the cation 2 to form in dilute solutions of $ZnBr_2$ in aqueous ethanol seems to be rather doubtful. Moreover, according to ref.4, methylenecyclobutane is one of the main products of tetrabromoneopentane reaction with sodium and, as it was shown earlier, 4 can be obtained with an excellent yield by the action of zinc powder on tribromoneopentanol benzenesulphonate[5]. The obvious impossibility of the classical mechanism for these reactions prompted us to reinvestigate the mechanism of the Gustavson rearrangement.

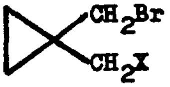
For this reason we have studied the reaction of tetrahaloneopentanes 1, 5, 6, esters 7 - 10 and their cyclopropyl analogs 11 - 14 with zinc dust[6].

$(CH_2Br)_3CCH_2X$

1, X=Br; 6, X=Cl;
7, X=OAc; 8, X=$OCOCH_2F$;
9, X=OSO_2Ph; 10, X=$OCOCF_3$

$C(CH_2I)_4$

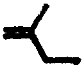
5



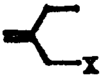
11, X=Br
12, X=OAc
13, X=$OCOCH_2F$
14, X=$OCOCF_3$

To a well-stirred suspension of 5g activated zinc dust in 50ml of refluxing 80% aqueous ethanol 8-10 mmoles of 1 or 5-14 was added, the reaction mixture was refluxed for 0.5-1 h, cooled and diluted with 10ml of n-octane. The mixture then was washed with 3x20ml of cold water and dried. The results of GLC analysis[7] are summarized in Table 1.

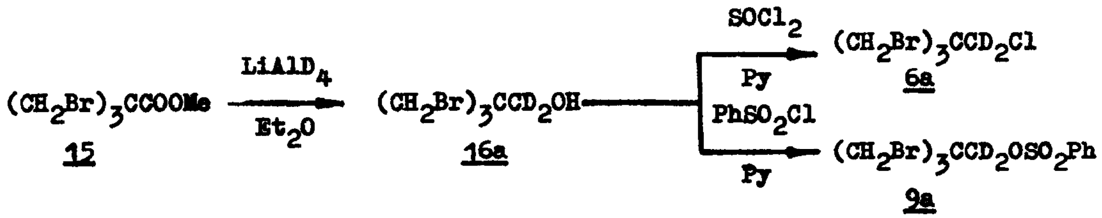
Table 1

Starting compound	Product distribution, % (total yields 60-80%)			
				
1 or 11	-	22	76	2
5	0.5	30.5	67.9	1.1
6	-	6.4	93.2	0.4
7 or 12	71[a]	14[b]	15	-
8 or 13	34[a]	3[b]	63	-
9	-	8.5	91.5	-
10 or 14	-	-	100	-

[a] corresponding 

[b] corresponding 

The data given in Table 1 seem to confirm the fact that the first step of the reaction of neopentane derivatives with zinc is not the rearrangement but the cyclization into the corresponding cyclopropane derivatives. At the same time the relative rate of methylenecyclobutane formation strongly depends on the leaving group X, and this rearrangement accelerates for highly electronegative groups, such as Cl, OSO_2Ph and $OCOCF_3$. This trend seems to speak in favour of the participation of CH_2X group in the ring expansion. To test this hypothesis, we have prepared the deuteroanalogs of 6 and 9 - 6a and 9a:

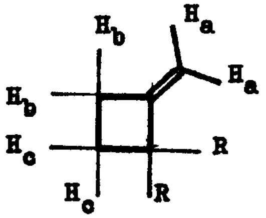


The $LiAlD_4$ reduction of methyl tribromopivalate 15[8] in ether yields 70% of 16a, b.p. 109–110°/2.5mm, ^1H NMR[9] : 3.70 (br.s, < 0.1 H, CHD), 3.53 (s, 6H, CH_2Br), 1.75 (br.s, 1 H, OH), which with $SOCl_2$ in pyridine gives 6a, yield 60%, m.p. 124–126° (subl.), ^1H NMR : 3.72 (br.s, < 0.1 H, CHD), 3.59 (s, 6H, CH_2Br), and the reaction of 16a with $PhSO_2Cl$ in pyridine leads to 9a, yield 80%, m.p. 80–80.5° (MeOH), ^1H NMR : 7.55–7.95 (m, 5H, Ph), 4.03 (br.s, < 0.1H, CHD), 3.48 (s, 6H, CH_2Br).

The reaction of 6a or 9a with zinc powder in refluxing ethanol gives mixtures of hydrocarbons (yields ca. 80%), containing > 90% of methylenecyclobutane-d_2 with deuterium localized exclusively at the C_2 atom (Table 2).

Table 2

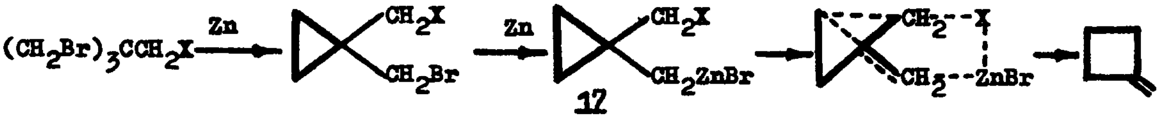
^1H NMR spectra[9] of



(4, R=H; 4a, R=D)

Starting compound		H_a	H_b (+R)	H_c
6 or 9	δ, ppm	4.55–4.66 m	2.53–2.77 t J=7.5 Hz	1.79–2.07 q J=7.5 Hz
	Relative intensity	1.0	2.0	1.0
6a or 9a	δ, ppm	4.56–4.63 m	2.53–2.77 t J=7.5 Hz	1.78–2.05 t J=7.5 Hz
	Relative intensity	1.0	1.1	1.0

Such a regioselectivity clearly contradicts the carbonium ion mechanism of Gustavson rearrangement[1], and seems to speak in favour of the participation of the organozinc intermediate 17:



The investigation of the reaction of 1 with other metals[10] strongly supports this conclusion. It seems necessary to note, that intermediate formation of organozinc compounds in protic media was recently demonstrated for the reactions of allyl bromide[11] and *gem*-dibromocyclopropanes[12] with zinc.

References and notes

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6. All new compounds give satisfactory spectral and analytical data; 6, m.p. 124–125° (purified by sublimation), 8, m.p. 48–49° (ethanol-ether), 10, b.p. 103–105°/1mm, n_D^{20} 1.5048.
7. 2.5m x 3mm column with 0.5% of PEG 2000 on NaCl or 6m x 3mm column with 15% of tris-(β-cyanethoxy)propane on Celite 545 or capillary column 25m x 0.25mm with triethyleneglycol dibutirate.
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9. The ^1H NMR spectra were determined at 100 MHz with Tesla BS-497 spectrometer for 20% solutions in CCl_4. The chemical shifts are expressed in δ-values (ppm) relative to a Me_4Si internal standart.
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