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# THE ACTION OF ALKALI ON CAGE CHLOROKETONES(1)

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We wish to report the successful ring-contraction, via Favorskii rearrangement, of the chlorinated pentacyclodecanones III and V, and the contrasting cleavage, under the same conditions, of the closely related XI and XVI. We began these experiments in the hope of synthesizing cubane derivatives, and a paper of Conia and Salaün served to point up the potential of the Favorskii rearrangement for constructing such strained molecules(2); subsequently, Eaton and Cole reported their elegant synthesis of cubane itself(3a), and other examples of the success(3b) and failure(3c) of this reaction in related systems have been described. Although we have not yet attained our original goal, current interest in cage molecules and our facile syntheses of several novel alicyclic systems prompt us to make this preliminary account.

Hydrolysis of dimeric 5,5-ethylenedioxytetrachlorocyclopentadiene(4) (I) with excess 96% sulfuric acid gives only the mono-ketone II* (m.p. 228-231°, $\nu_{C=O}^{CH_2Cl_2}$ 1748 cm$^{-1}$, $\nu_{C=C}$ 1603 and

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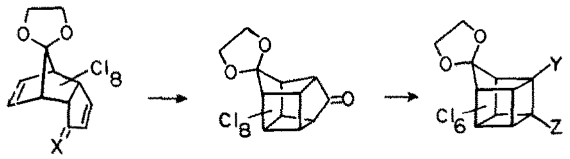
* Satisfactory elemental analyses (C, H, Cl) were secured for all new compounds described.

1590 $cm^{-1}$, C-H absorption ca. 2900 and 1470 $cm^{-1}$). Irradiation, through Pyrex, of a solution of II in dichloromethane brings about quantitative isomerization to the cage isomer III(5) ($\nu_{C=O}^{CH_2Cl_2}$ 1820 $cm^{-1}$; no absorption 1800-1400 $cm^{-1}$).

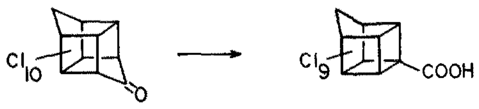
Reaction of III with its own weight of potassium hydroxide (85%) pellets in refluxing xylene, or less conveniently with excess refluxing 10% aqueous potassium hydroxide, transforms it (95% overall yield from I) into a single saturated carboxylic acid, IV (m.p. 286° dec.; methyl ester, m.p. 154-155°, $\nu_{C=O}^{CCl_4}$ 1750 $cm^{-1}$; no absorption 1500-1700 $cm^{-1}$, $\lambda_{max} < 210$ mμ, $\epsilon_{210}^{EtOH}$ 600*).



I, X = $(-OCH_2)_2$ III IVa, Y = Cl, Z = COOH

II, X = O IVb, Y = COOH, Z = Cl

Prolonged treatment of the similar cage perchloroketone V(7), under the same conditions, converts it in good (~ 85%) yield to another saturated acid, VI (m.p. ca. 320° dec., $\epsilon_{210}^{MeOH}$ 480; methyl ester, m.p. 162-163°); V was reported to be stable to base(7a).



V VI

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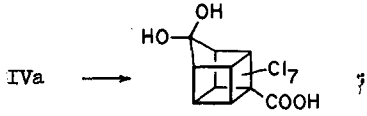
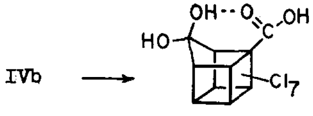
* Even isolated double bonds bearing two vinylic chlorines have intense absorption ($\epsilon$ about $10^4$) near 220 mμ(6).

Although the symmetry of V permits only a single Favorskii rearrangement product, acid IV might _a priori_ bear the carboxyl at either C.3 (IVa) or at C.2 (IVb)*. "Hydrolysis" of IV with fuming (15% $SO_3$) sulfuric acid or oxidation with boiling concentrated nitric acid effects removal of the ethylene glycol residue and furnishes the hydrated keto-acid VII in ~ 80% yield. Examination of models indicates that one of the rather acidic hydroxyl groups** of VIIb is within hydrogen-bonding distance (O-O distance ~ 2.8 Å) of the carboxyl at C.2, so should enhance markedly the acidity of VIIb, versus IVb, whereas in VIIa no such bonding is possible.



VIIa



VIIb

We have measured the acidities of these substances in 50% aqueous ethanol (potentiometric titration; electrodes calibrated in aqueous buffer) and obtained the following data: (pKa ± 0.05) VI, 3.02; IV, 3.54; VII, 3.67. This result allows us

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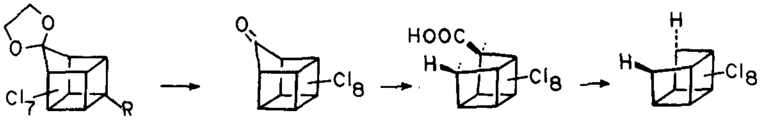
* The systematic name of IV is 6,6-ethylenedioxyheptachloropentacyclo[5.2.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$]nonane-3-carboxylic acid (a "homocubane"); III is 4,4-ethylenedioxyoctachloropentacyclo-[6.2.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]decan-7-one; XII is 4-_endo_-H-octachlorotetracyclo[4.2.0.$0^{2,5}$.$0^{3,8}$]octane-4-_endo_-carboxylic acid; and XVII is 7-H-3,6-bis-(_endo_-carbomethoxy)-heptachlorotricyclo-[2.2.2.$0^{2,5}$]oct-2-ene.

** Compounds III, V and XI form stable hydrates from which they are regenerated with difficulty; V exhibits a pKa′ of _ca_. 9.9 in 50% aqueous ethanol.

to assign structure a to IV and is supported by our failure to resolve IV; IVa possesses a plane of symmetry (passing diagonally through the body of the "cube", and including the bridge and carboxyl carbons) while IVb does not. Exclusive formation of IVa may be rationalized by noting a severe non-bonding interaction in III between the upper chlorine α to the carbonyl, and the adjacent oxygen, relieved in IVa but made worse in the initial stages of rearrangement to IVb.

Successive reaction of IVa with thionyl chloride, sodium azide in boiling xylene, and benzyl alcohol, followed by hydrogenolysis of the benzyl urethan (VIII, m.p. 191-192°) furnished an amine, IX (m.p. ~ 260° dec.) in about 50% overall yield. Deamination of IX with nitrosyl chloride gave the chloride(8) (X, 85%, m.p. 265-266°), and hydrolysis of the latter with 15% oleum provided the perchloroketone XI ($\nu^{CS_2}_{C=O}$ 1815 $cm^{-1}$), isolated as the hydrate. Reaction of XI with 10% aqueous potassium hydroxide furnished a carboxylic acid (XII) isomeric with XI-hydrate. The p.m.r. spectrum (in deuteriochloroform) of its methyl ester (XIII, m.p. 175.5-178°) revealed, besides a singlet (3 H) at 6.09 τ assigned to the methoxyl, a singlet (1 H) at 5.20 τ. Decarboxylation of XII, at 130° in sulfolane containing a trace of collidine, gave (50%) of a saturated substance $C_8H_2Cl_8$ (XIV, m.p. 189-191°, $\lambda_{max} < 210$ mμ, $\epsilon^{EtOH}_{210}$ 360, no infrared absorption 1400-2000 $cm^{-1}$), the p.m.r. spectrum of which possessed only a single sharp line at 4.78 τ ($J_{C^{13}-H}$ 158 cps, singlet satellites).(9)



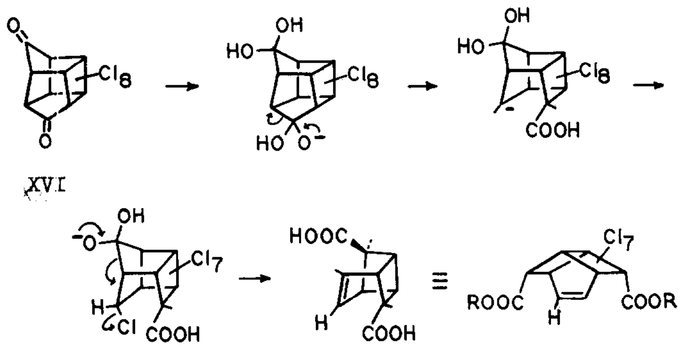
IVa, R = COOH　　XI　　XII　　**XIV**

IX, R = $NH_2$

X, R = Cl

Although the stereochemistry of XIII and XIV is unproven, we have assigned the configurations shown from the relatively normal C-H stretching frequency observed for XIV ($\nu_{C-H}^{CS_2}$ 2970 cm$^{-1}$), indicating the absence of severe H-H opposition$^{(10)}$, and on the assumption that the carbanions preceding XII and XIV would be protonated from the less-hindered exo side$^{(11)}$.

Reaction of VII with aqueous alkali gives a tetracyclic diacid analogous to XII, characterized as its dimethyl ester (XV, m.p. 134-136°, $\nu_{C=O}$ 1757 cm$^{-1}$; 5.16 $\tau$ (1 H, s.), 6.08 $\tau$ (3 H, s.), 6.15 $\tau$ (3H, s.); these data do not distinguish between the two possible isomers. When the same reaction conditions were applied to the cage diketone XVI$^{(7c,12)}$, we isolated (in about 50% yield after esterification and chromatography) not the expected XV, but an isomeric diester (XVII, m.p. 117.2-118.5°) having an olefinic hydrogen and infrared- and p.m.r.-equivalent carbomethoxyl groups ($\nu_{C=O}^{C_2Cl_4}$ 1760, $\nu_{C=C}$ 1607 cm$^{-1}$; 3.53 $\tau$ (1 H, s.), 6.20 (6 H, s.); $\lambda_{max}^{EtOH}$ 290 (108); $\epsilon_{210}$ 8500). We have assigned to it the structure shown, based on the following plausible mechanism:



XVI

XVII, R = $CH_3$

Obtention of cleavage products (XII, XV and XVII) raises the possibility that the "rearrangement" products arise by cleavage and subsequent reclosure with displacement of chloride, the chlorocarbanion being discharged and reformed reversibly; this point, as well as the further transformations of these interesting substances, is being investigated.

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1 Supported in part by the Petroleum Research Fund, administered by the American Chemical Society; grateful acknowledgement is made to the donors of the Fund. We are indebted to Allied Chemical Corp. for a gift of compound V, and to Mr. Stanley Rhodes for preparative assistance. A partial account of this work was presented at the 147th Meeting of the American Chemical Society, Philadelphia, Pa., April 1964; abstracts, p. 23N.

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