

Our results emphasize a useful rule relating to RNA-DNA hybridization experiments with mammalian nucleic acids. With our source, *viz.* developing foetal erythroid cells, greater stringency of reaction conditions was achieved with formamide and low temperature. Within the range of experimental conditions used by us, the main conclusion drawn from the experiments remained unaltered when mismatching of hybrids was avoided in this way. Transcriptional activity decreased in these cells as the process of specialization proceeded. Hence we conclude that differentiation in these cells is accompanied by increasing repression of the genome.

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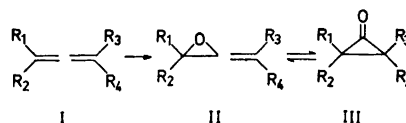
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Attempts to Prepare Halogenated Cyclopropanones

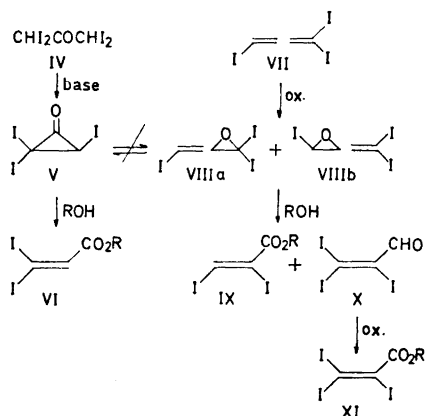
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Since 1951, when Loftfield proposed that cyclopropanones are intermediates in the Favorsky rearrangement, these ring compounds have been of special interest to organic chemists.¹ Several attempts have been made to synthesize them, but until very recently all these experiments have failed. In 1966 Hammond and Turro succeeded in preparing cyclopropanone and 2,2-dimethylcyclopropanone by the action of diazomethane on ketene and dimethylketene. These compounds were reported to be highly unstable, and reacted at low temperatures with acids, bases and alcohols.^{2,3} In 1968 Crandall and Machleder reported that the stable 2,2-di-*t*-butylcyclopropanone (IIIa) could be isolated from the peracid oxidation of 1,1-di-*t*-butylallene (Ia).⁴ The authors consider



	R ₁	R ₂	R ₃	R ₄
a.	<i>t</i> -Bu	<i>t</i> -Bu	H	H
b.	<i>t</i> -Bu	H	<i>t</i> -Bu	H
c.	<i>t</i> -Bu	<i>t</i> -Bu	<i>t</i> -Bu	H



the allene oxide IIa to be an intermediate in this reaction, but due to the fact that IIIa is thermodynamically favoured over IIa, the cyclopropanone IIIa is isolated.

In 1968 Camp and Greene isolated the allene oxide IIb from the peracid oxidation of 1,3-di-*t*-butylallene (Ib). They reported that IIb on heating did isomerize to the cyclopropanone IIIb.⁵

The rearrangement of 1,1,3,3-tetraiodoacetone (IV) is reported to yield 3,3-diiodoacrylic acid (VI) and this rearrangement is considered to pass *via* the triiodo-cyclopropanone V; *vide infra*.⁶ In analogy with the preparation of IIIa and IIIb, another possible route to VI would be the peracid oxidation of triiodoallene (VII).

Kai and Seki have recently described the synthesis and the air oxidation of triiodoallene and tetraiodoallene.⁷⁻⁹ From the air oxidation of triiodoallene (VII) in aqueous THF or in alcohol, they isolated *Z*-2,3-diiodoacrylic acid (IX) or its ester and triiodoacrolein (X). In this reaction they consider the allene oxides VIIIa and VIIIb to be intermediates.⁸ The products in this oxidation is different from that of the Favorsky rearrangement of IV.⁶

Experiments have been performed to oxidize the triiodoallene VII with peracetic acid in absolute ether. The reaction products were then treated with aqueous dioxane. The acidic components were separated using TLC and identified with authentic samples.⁶ Comparison revealed that IX and XI but not 3,3-diiodoacrylic acid had been formed. The triiodoacrolein formed by the air oxidation of triiodoallene by the method of Kai and Seki, was isolated as 2,3,3-triiodoacrylic acid (XI) due to further oxidation.

Since the resulting products in the two reactions under discussion are different they cannot be formed *via* the same intermediate. The question now arises as to which reaction is the most probable one to pass *via* the cyclopropanone V. Rappe isolated 3,3-dichloro-2-methacrylic acid from the Favorsky rearrangement of 1,1-dichloro-3,3-dibromobutanone-2. This accounts for a cyclopropanone as intermediate, and up to now, though somewhat questionable, the cyclopropanone mechanism seems to be the most plausible one for the rearrangement of tetrahalo-ketones.¹⁵ Kai and Seki do not discuss whether a cyclopropanone could be an intermediate in the air oxidation of triiodoallene. Such an intermediate could explain the stereoselective formation of

Z-2,3-diiodoacrylic acid (IX) but not the formation of triiodoacrolein. Thus it is reasonable to assume that the cyclopropanone V is not an intermediate in this case. This is contrary to the behavior of the nonhalogenated allene oxides IIa and IIb.

An explanation for the failure of VIIIa and b to isomerize to the cyclopropanone V could be an unfavorable position of the equilibrium between the allene oxide and the cyclopropanone, due to steric hindrance. This is in agreement with Crandall and Machleder's findings that tri-*t*-butylallene oxide IIc, obtained from the peracid oxidation of Ic was extraordinarily stable and failed to isomerize to the cyclopropanone IIIc.¹⁶ The authors explained this deviation from the expected equilibrium as being due to steric repulsion of the eclipsed vicinal *t*-butyl groups.

If, on the other hand, the allene oxides VIIIa and b are the actual reaction intermediates, as proposed by Kai and Seki, an anomalous stability against water would be called for. Thus allene oxides are known to add water under cleavage of the ring to form α -hydroxyketones.¹⁷ Even though the mechanism proposed by Kai and Seki, involving halogen migration to form the corresponding acryloyl iodides or triiodoacrolein, fully explains the formation of the reaction products, more work is needed to clarify the identity of the actual reaction intermediate.

Attempts were also made to oxidize tribromoallene with peracetic acid as an analogous route to the tribromosubstituted cyclopropanone. The acidic products formed were analyzed by TLC and MS on the TLC scrapings. Comparison revealed that no 3,3-dibromoacrylic acid, which is the product from the Favorsky rearrangement of 1,1,3,3-tetrabromoacetone,⁶ had been formed. The products formed, *viz.* *Z*-2,3-dibromoacrylic acid and 2,3,3-tribromoacrylic acid, are analogous with the corresponding iodo acids formed by the oxidation of triiodoallene.

Experimental. Thin Layer Chromatography was performed as described by Rappe and Andersson.⁶ Mass spectra were recorded on an LKB 9000 mass spectrometer on TLC scrapings, which in every case gave rise to a parent peak at $M^+ - CO_2$. *Triiodoallene* was prepared according to Kai and Seki, although not in a comparable quantity to that stated by these authors.⁸ It was found, however, that some important details were omitted in their

original description. The correct description for the preparation of triiodoallene appears in their patent pending for that compound.¹⁰ *Tribromoallene* was synthesized by the method of Roedig and Detzer and involved alkali cleavage of perbromocyclopent-1-ene-3,4-dione (xanthogallol).¹¹ *Z-2,3-Diiodoacrylic acid* was prepared by the air oxidation of triiodoallene in aqueous THF as described by Kai and Seki.⁸

Oxidation of triiodoallene using peracetic acid. In each case, an equivalent quantity of peracetic acid, suitably diluted with absolute ether, was added to the chilled (0°C) ethereal solution of the allene, and the mixture kept stirred at 0°C for 4 h. A convenient volume of a mixture of dioxane and water (1:1) was added to produce a homogeneous solution, and stirring was maintained for 16 h at room temperature. Aqueous NaHCO₃ was then added until the mixture was alkaline. The mixture was shaken with ether, the ethereal layer being rejected. The aqueous layer was then acidified with dilute sulphuric acid. The solution was extracted with ether, the ethereal layer dried (MgSO₄) and concentrated. TLC was then carried out on the ethereal solution. As authentic samples we used 3,3-diiodoacrylic acid,¹² *Z-2,3-diiodoacrylic acid*,⁸ and 2,3,3-triiodoacrylic acid,¹² all in ethereal solutions.

In agreement with Kai and Seki's findings, only two spots with the same *R_F*-values as *Z-2,3-diiodoacrylic acid* (higher) and 2,3,3-triiodoacrylic acid (lower) were obtained. The identity was further verified using MS on the TLC scrapings.

Oxidation of tribromoallene. Working on an estimated yield of 80% of tribromoallene (Roedig and Detzer obtained a yield of 78.5%), an equivalent amount of peracetic acid, suitably diluted with absolute ether and chilled to -80°C, was added. The mixture was kept stirred at -80°C for 4 h, then at room temperature for 24 h. A convenient volume of a mixture of dioxane and water (1:1) was then added until a homogeneous solution was obtained, and the mixture stirred for another 24 h. Aqueous NaHCO₃ was added until the mixture was alkaline. The mixture was washed with ether, acidified with dilute sulphuric acid and extracted with ether. The ethereal layer was dried (MgSO₄) and concentrated. TLC

was carried out on the ethereal solution obtained, 3,3-dibromoacrylic acid,¹⁴ *Z-2,3-dibromoacrylic acid*,¹⁴ and 2,3,3-tribromoacrylic acid¹³ being used as standards. The experimental ethereal solution gave rise to two spots which on comparing *R_F*-values and MS fragmentation of the scrapings, were found to correspond to *Z-2,3-dibromoacrylic acid* (higher) and 2,3,3-tribromoacrylic acid (lower).

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