FREE RADICAL TELOMERIZATION OF VINYLENE CARBONATE (1,3-DIOXOL-2-ONE) WITH POLYHALOMETHANES --- CHEMISTRY AND SYNTHETIC APPLICATIONS OF TELOMERS ---

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Abstract: Free-radical telomerization of vinylene carbonate (1,3-dioxol-2-one) in the medium of polyhalomethanes proceeds smoothly to result in the stereoselective formation of type $\underset{\sim}{2}$ telomers, among which lower products ($n \leqq 3$) are obtainable in high stereohomogeneity and may serve as versatile intermediates for the synthesis of polyalcohols including carbohydrates and related compounds of biological significance. Preparation and chemistry of the title telomers, and their potential as synthetic intermediates are surveyed from a preparative point of view.

IV Miscellaneous Reactions

IV-1 Dehydrohalogenation

IV-2 Dehalogenative Reduction

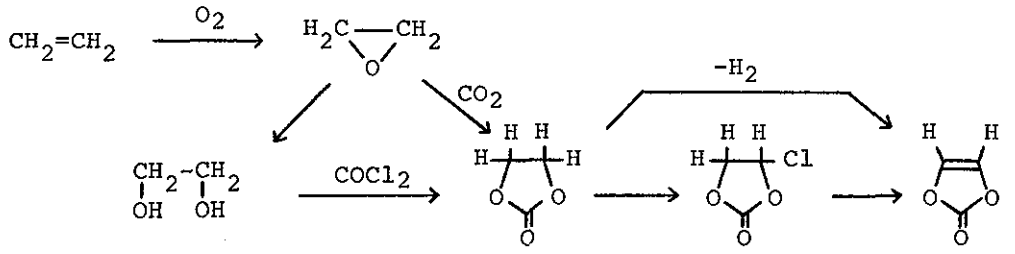
IV-3 Nucleophilic Substitution

Polymerization in the presence of a chain transfer agent to yield a series of low molecular weight products is termed telomerization,[1] which can be formally described by

$$\underset{\substack{\text{taxogen}\\(\text{monomer})}}{M} + \underset{\text{telogen}}{A\text{-}B} \xrightarrow{\text{initiator}} \underset{\text{telomer}}{A\text{-}M_n\text{-}B}$$

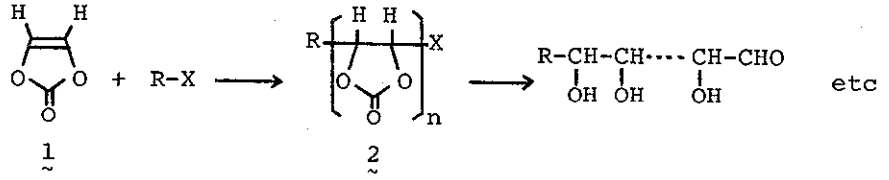
In principle, it is possible to obtain any average chain length distribution desired simply by adjustment of the ratio of telogen to taxogen, and telomers are primarily characterized by α,ω-disubstituted functional groups derived from telogen. One of the most important features of this type of reactions in organic chemistry may be the synthetic potential as a unique one-step route to mono-, di- and poly-functional compounds not easily otherwise accessible. Much work has been devoted to this field of study since the first reports[2] in the 1940's, and increasing numbers of papers including reviews on various aspects of telomerization reflect the continuing importance and interest in current chemistry.

Five-membered heterocycle, vinylene carbonate (1,3-dioxol-2-one) has been known as the parent compound of the series since 1953,[3] and commercially prepared from ethylene via ethylene oxide and ethylene carbonate. Substituted and non-substituted vinylene carbonates have been extensively investigated as the reactants in thermal[4] and



photochemical[5] cycloadditions as well as in homo- and co-polymerizations.[6] Thionocarbonates have also been an object of synthetic utilization.[7] This parent cyclic carbonate of cis-enediol structure exceptionally undergoes a smooth radical polymerization to give a high molecular weight homopolymer,[3] in strong contrast with other internal olefines like maleic anhydride and stilbene.

Free radical reaction of vinylene carbonate controlled in a molecular weight range by telomerization in the medium of polyhalomethanes would provide a novel type of telomer 2 as versatile intermediates for the preparation of biologically interesting polyalcohols including carbohydrates.



This type of telomerization which permits simultaneous introduction of protected α-hydroxyaldehyde function, has been found to smoothly proceed to result in the stereoselective formation of the telomers,[8] among which lower products (n≦3) are readily separable by chromatography on silica gel into one isomer as n=1, two isomers as

n=2 and four isomers as n=3 products. Such a selectivity is commonly observed in all instances examined, while attempts to separate higher telomers (n≧4) in stereohomogeneity have been unsuccessful.

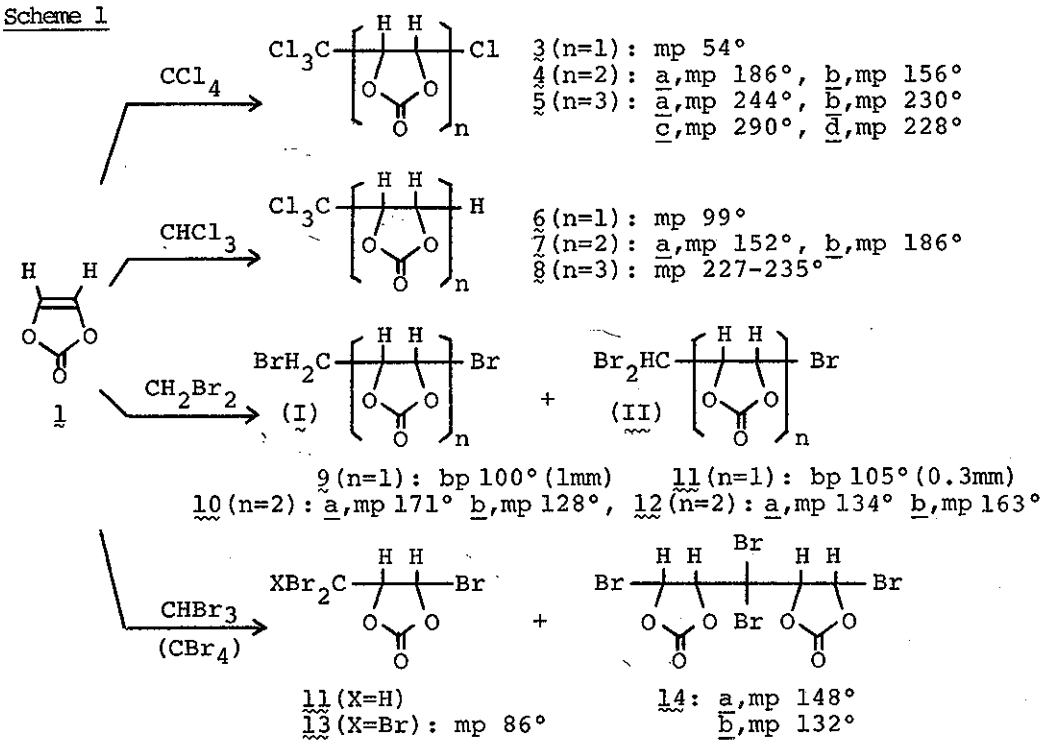
Utilization of the conventional non-carbon-centered telogens[1] involving oxygen, nitrogen, sulfur, phosphorous and silicon, and organometallic compounds, other than polyhalomethanes described here will be alternative interesting subject as a potential route leading to the compounds of special interest.

The present progress report deals with the mainly preparative results obtained so far with the type 2 telomers, particularly lower products with n value less than four, arising from free radical reaction of vinylene carbonate as a taxogen and polyhalomethanes as an excellent telogen.[9]

I. Telomerization Products

Vinylene carbonate undergoes the smooth telomerization with polyhalomethanes in the presence of benzoyl peroxide (BPO) or azobisisobutyronitrile (ABIN) as a radical initiator under a nitrogen atmosphere to give the telomers like 2 in yields depending on the conditions.[8] The telogens studied here involve carbon tetrachloride, chloroform, carbon tetrabromide, bromoform and methylene bromide to give the corresponding series of telomers (Scheme 1). As seen in Table I, a telomer distribution in this chain transfer reaction is remarkably affected, as might be expected, by the ratio of vinylene carbonate to polyhalides. Treatment of the reaction mixture with hot methylene chloride gives as the insoluble portion higher telomers

Scheme 1



with average n value of ten or higher, in addition to the soluble products which mainly consist of lower telomers ($n \leqq 4$). Column chromatography on silica gel[8a] offers an effective means for the separation of lower products into the stereohomogeneous isomers.

The vinylene carbonate-carbon tetrachloride system to give a single series of telomers with few side reaction products provides a good example of the common features encountered in telomerization and is discussed in more detail through the article for illustrative purposes.

Among several possible isomers, one, two and four isomeric telomers can be preferentially isolated as n=1, n=2 and n=3 products,

Table I. Isolated Yields (%) of Vinylene Carbonate Telomers[a)]

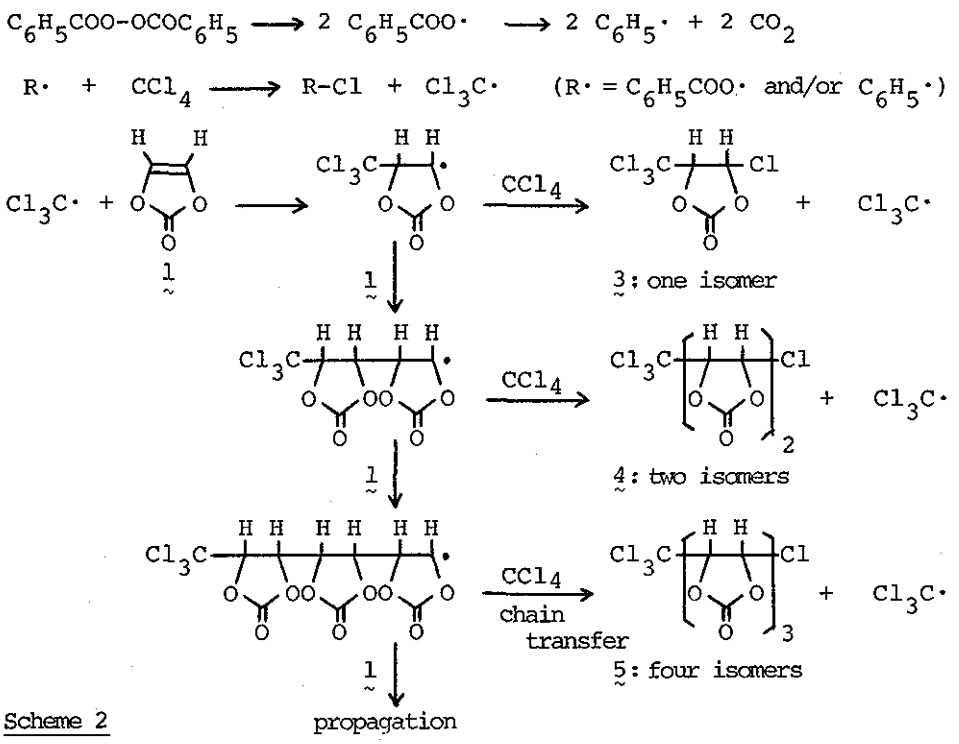
Mole ratio (telogen:1)	Telogen	Lower telomers n=1	Lower telomers n=2	Lower telomers n=3	Higher telomers[b)]
3	CCl_4	4.9 (3)	4.2 (4)	1.4 (5)	43.0 (n=15.5)
5	CCl_4	20.4 (3)	18.0 (4)	6.0 (5)	
7	CCl_4	28.5 (3)	15.6 (4)	3.6 (5)	15.4 (n=8.5)
12	CCl_4	45.3 (3)	12.2 (4)		4.9 (n=6.5)
8	$CHCl_3$	1.1 (6)	1.4 (7)		61.0 (n=17.5)
20	$CHCl_3$	4.8 (6)	6.3 (7)		4.3 (n=12.5)
25	$CHCl_3$	15.9 (6)	10.3 (7)	2.6 (8)	5.4 (n=10.5)
4	$CBrCl_3$	92.0[c)]			
15	CH_2Br_2	19.5 (9,11)	4.8 (10,12)		
5	$CHBr_3$	41.0 (11,13)	17.0 (14)		
2	CBr_4	39.0 (13)	11.0 (14)		

a) benzoyl peroxide as an initiator. b) insoluble products in hot CH_2Cl_2. c) 5-bromo-4-(trichloromethyl)-1,3-dioxolan-2-one.

respectively, which have been fully characterized spectroscopically and by elemental composition (Scheme 2). The stereohomogeneity is well established by spectral and chromatographic behaviors. The n=4 telomer is also isolated, presumably in an isomeric mixture.

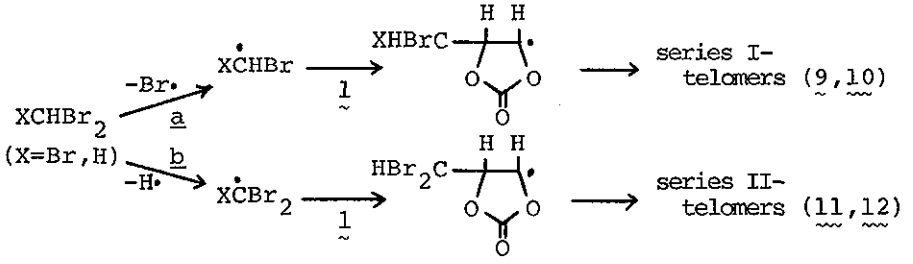
A similar stereochemical result has been observed with the telomerization with chloroform as a telogen, in which hydrogen transfer predominates, while bromoform reacts exclusively by bromine transfer as shown below.

When methylene bromide (or bromoform) is used as a telogen, the reaction is more complicated to yield significant quantities of the unusual series of telomers (II) in addition to the expected normal ones (I). In contrast to the general observation with the tendency[10] towards exclusive bromine abstraction, hydrogen and bromine may be



Scheme 2

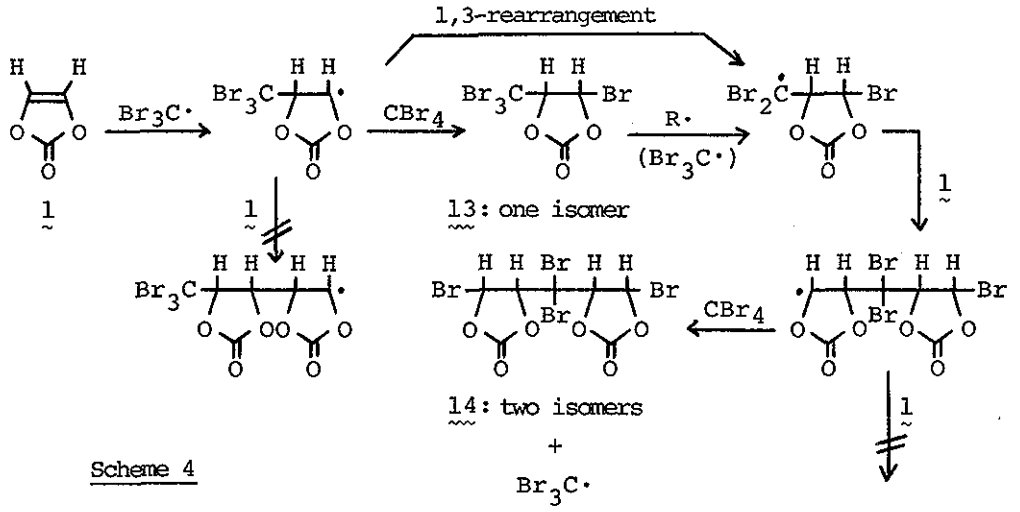
equally abstracted from the bromo-telogen by the initiator-derived radicals, resulting in two kinds of bromomethyl radicals. The subsequent propagation and chain transfer steps (as illustrated in Scheme 2) lead to an isolation of two different series (I and II) of



Scheme 3

telomers. Path b provides a very rare example of hydrogen abstraction from methylene bromide and bromoform by the peroxide-derived radicals[11](Scheme 3). Type II telomers can be easily converted to the type I series by nickel tetracarbonyl in tetrahydrofuran.[12]

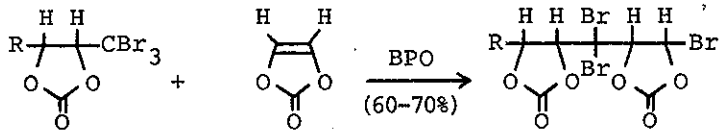
Telogens with high chain transfer coefficients such as carbon tetrabromide and bromoform give exclusively another type of n=2 telomers together with n=1 adduct and no product of type 2 (n≧2) is formed except at extremely high ratio of vinylene carbonate to telogen.[8,13] Secondary telomerization commonly observed in which primary telomer (n=1) functions as more active secondary telogen than



Scheme 4

original agent,[2a] may chiefly contribute to the formation of such n=2 products which can no longer work as telogen, though another possibility involving 1,3-radical rearrangement cannot be precluded (Scheme 4).

Thus, type 16 compounds[13] are readily available by free-radical reaction of compounds 15 and vinylene carbonate (1), and the reaction is generally applicable to 1,1,1-tribromomethyl compounds.



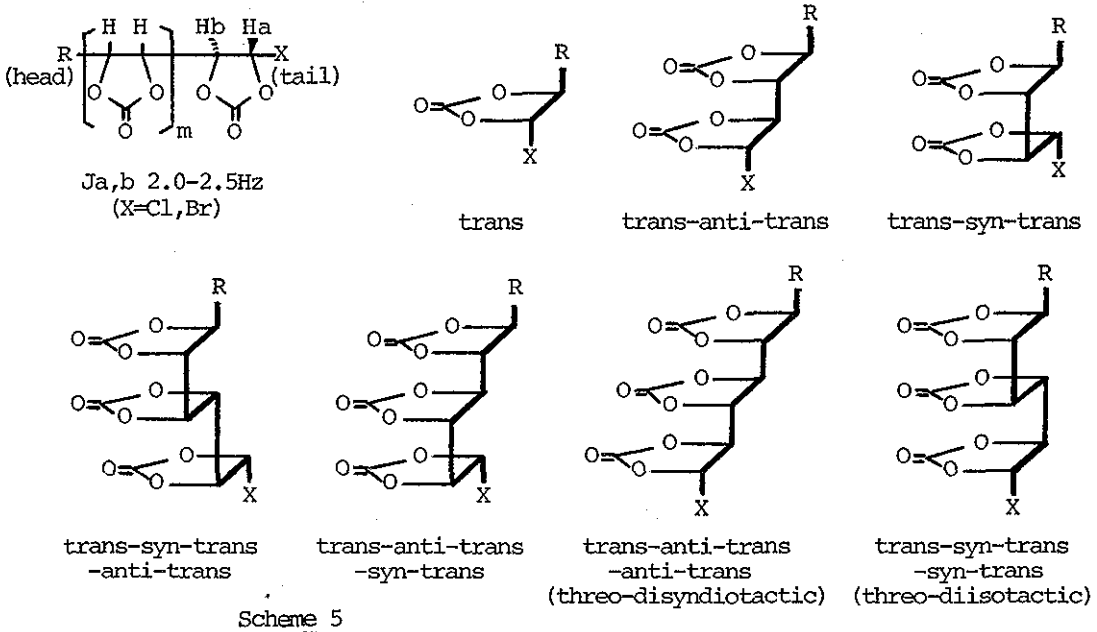
15 (R=Br, CN, COOMe) 1 16 (two isomers)

Use of bromotrichloromethane as a telogen results in the exclusive formation of the 1:1 adduct 3' (2, n=1, R=CCl_3, X=Br).

II. Stereochemistry of Telomers

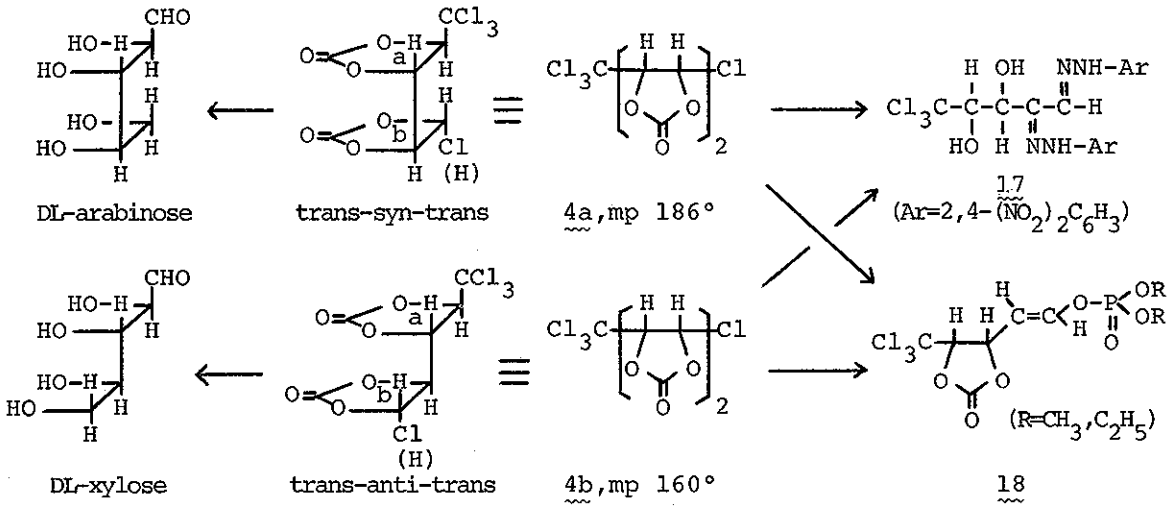
Steric factors play the most important part in the stereoselective formation of the telomers during free-radical telomerization. Preferential formation of trans-addition products might be expected in the rather nonflexible cyclic carbonate system, because the eclipsing approarch of telogens to the halogenomethyl-substituted carbonate radicals in the product-forming step of the chain transfer process is energetically much disfavored.[14]

Just as predicted on the kinetic viewpoint, the trans-stereochemistry of all the n=1 products isolated except 6 is substantiated by the small coupling constants, Jvic 1.5-2.5Hz, between the vicinal protons on the five-membered carbonate rings, which are in good accord with the value of monochloroethylene carbonate (J=2.0Hz, J'=5.5Hz), attributable to trans coupling, whose assignment rests on the premise (considered reasonable) that Jcis>Jtrans.[15] All of the n=2 and n=3 telomers isolated (except the products from chloroform telogen) show well-defined doublet peaks due to Ha protons with small coupling constants, Ja,b=2.0-2.5Hz, comparable to those of the n=1 adducts.[8]

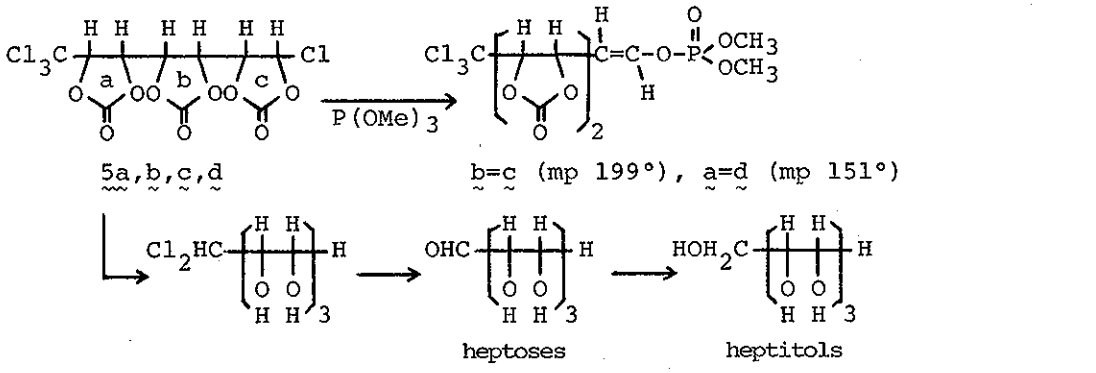


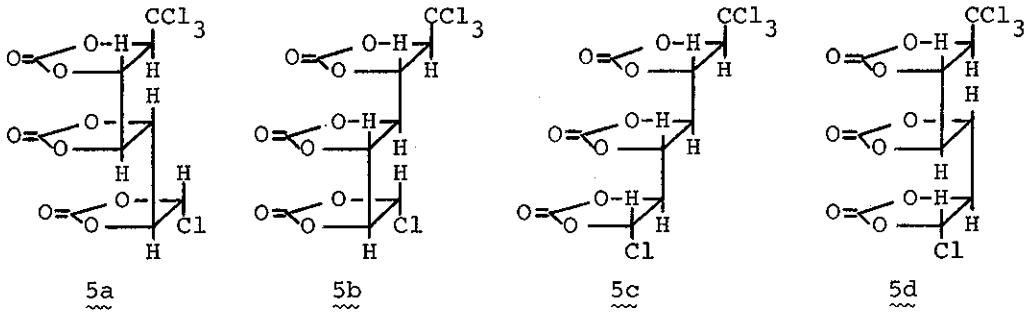
Scheme 5

Application of the general tendency observed with the n=1 series to the n=2 and 3 telomers predicts two and four structures, respectively, which are defined in the present article by the terms"trans-syn" and "trans-anti" for convenience (Scheme 5). Such a geometry with respects to the carbon skelton is unequivocally proven by chemical transformation to the authentic aldoses. Stereoisomeric n=2 telomers, 4a,b, form the identical derivatives of phenylosazone 17[8] and enol-phosphates 18,[16] indicative of configurational difference at the carbonate ring b. Further, telomers 4a and b, as well as 7a and b from chloroform telogen, can be converted to DL-arabinose and -xylose,[17] respectively, by the procedure described below involving conversion of trichloromethyl group into formyl function and thus, trans-"syn"-trans and trans-"anti"-trans configurations



Scheme 6





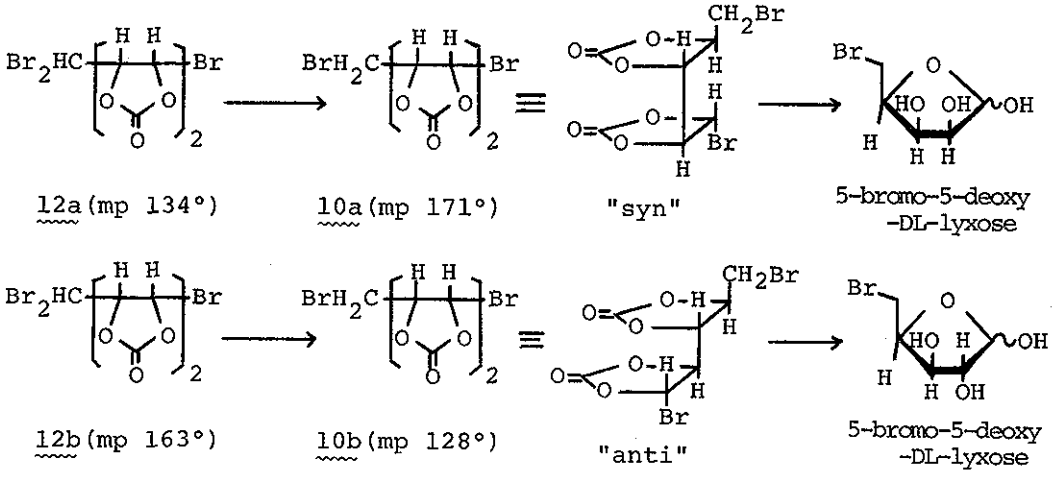
Scheme 7

have been clearly established (Scheme 6).

In the similar way, four n=3 telomers, 5a,b,c and d are configurationally assigned as "syn-anti", "anti-syn", "anti-anti", and "syn-syn" structures, respectively, by the transformation into heptitols via heptoses and to enol-phosphates (Scheme 7)[18], that is, heptitols derived from 5a, b, c and d are gaschromatographically identical with the authentic specimens[19], D-glycero-L-galacto-, D-glycero-D-ido, meso-glycero-ido- and D-glycero-D-galacto-heptitols, respectively, and 5b and 5c as well as 5a and 5d are a pair of stereoisomers differing only at the ring c configurations.

Thus, the free radical telomerization with polychloromethanes has been ascertained to proceed exclusively in trans-fashion.

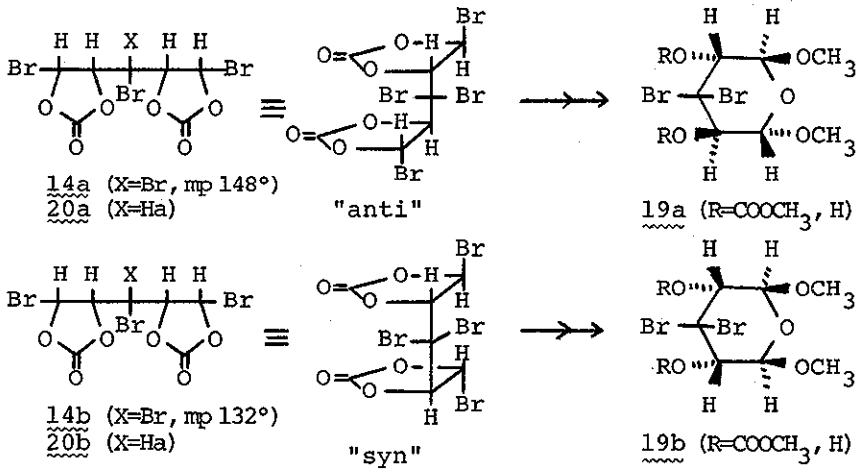
The n=2 telomers from methylene bromide are also shown trans addition products by selective reduction of 12a and b with nickel carbonyl in tetrahydrofuran[12] to 10a and b followed by mild hydrolysis into 5-bromo-5-deoxy-DL-lyxose and -xylose[8], respectively (Scheme 8).



Scheme 8

The identity is established by chromatographic comparison with the authentic specimens prepared conventionally from D-mannose and D-xylose.[8] Thorough hydrolysis of 10a,b to lyxose and xylose is not employed intentionally for fear of the epimerization under more severe hydrolytic conditions.

There remains ambiguity about the stereochemistry of the isomeric "two-fold addition"products 14a and b for which meso(trans-"syn"-trans)- and dl(trans-"anti"-trans)-forms are anticipated.[13a] Methanolysis of 14a and b to the cyclic hemiacetals followed by methylation yields 19a and b, of which nmr analysis permits configurational assignment of the telomers as dl- and meso-forms.[13] These configurations are further supported by the reductive to photolysis in tetrahydrofuran to 20a and 20b, of which latter shows a clear-cut triplet signal due to Ha proton in the nmr spectrum, in contrast to doublet-doublet peak of 20a (Scheme 9).



Scheme 9

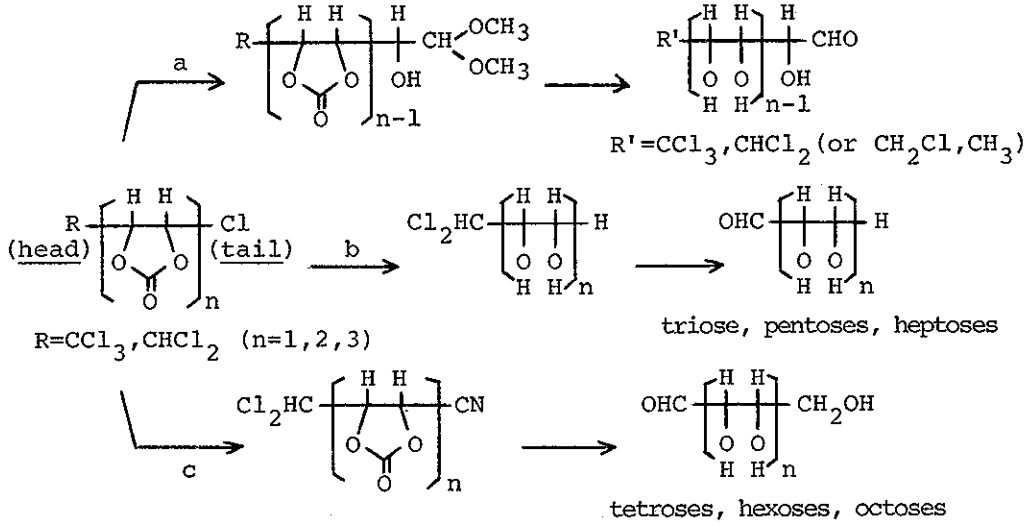
The above findings demonstrate conclusively that a free-radical telomerization of vinylene carbonate with polyhalomethanes leads to selective formation of the exclusive trans-addition telomers.

III Synthetic Applications

III-1. Aldo-sugars (Triose to Octoses)

Apart from chemical modifications of naturally occuring monosaccharides, total synthesis of carbohydrates from simple non-sugar substances mostly involves non-specific and long processes at the stage of the chain extension or introduction of functional groups as in the formose synthesis[21] and others.[22] As readily expected from the telomer structures, this type of telomerization is of significance in the potential utility for stereoselective synthesis of higher aldosugars from simple achiral compounds.

Either head or tail carbon of the telomers can be altered to carbonyl function to afford a series of "odd-carbon" sugars by the routes (a and b), involving mild hydrolysis via the acetals or reduction to

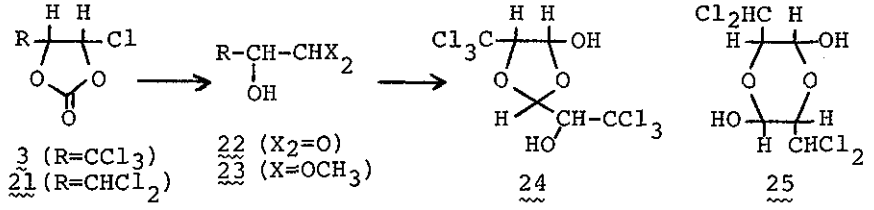


Scheme 10

the dichloro compounds followed by hydrolysis, and substitution of tail halogen with C_1-unit opens up the route to the "even-carbon" aldoses (route c). Scheme 10 outlines the general routes from vinylene carbonate telomers to aldoses, among which halogenated ones may be the verstile intermediates for thio-, amino-, unsaturated and deoxy-sugars, since trihalomethyl moiety is stepwise convertible to methyl group through lower halide by the available methods.[12,20,23] Consequently, total synthesis of monosaccharide from ethylene has become feasible.

i. triose from n=1 products: Photolysis in tetrahydrofuran[20] seems to be the method of choice for selective conversion of the trichloromethyl groups to the dichloromethyls in the labile compounds like the telomers. Nickel carbonyl is satisfactory agent for this purpose as well.[12] Irradiation of the n=1 adduct with high pressure Hg-lamp gives high yield of the dichloromethyl compound (21), which can be converted into DL-glyceraldehyde by the successive treatment with borohydride and silver nitrate,[17a] though in poor yield[17] (route b).

On the other hand, by standing aqueous solutions at room temperature, n=1 telomer is quantitatively hydrolyzed to 3-deoxy-glyceraldehyde (22, R=CCl_3) which dimerizes selectively to five membered ring compound 24, characterized as diacetate, while the dichloromethyl derivative 21 preferentially forms six-membered cyclic dimer 25. Treatment of 3 with methanol gives high yield of the acetal 23.



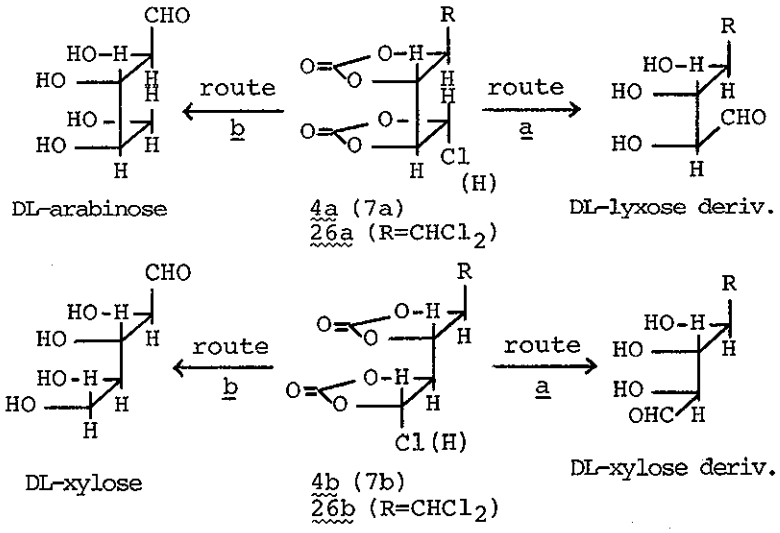
3 (R=CCl_3)
21 (R=$CHCl_2$)

22 (X_2=O)
23 (X=OCH_3)

24

25

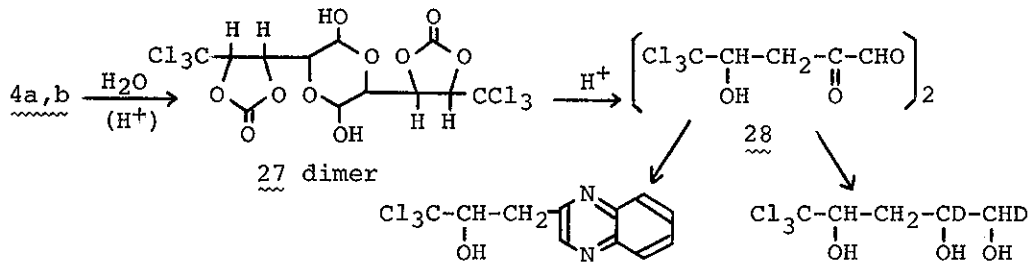
ii. pentoses from n=2 telomers: Photo-reduction of 4a and 4b gives high yields (~80%) of the dichloromethyl compounds 26a and b which can be converted in the conventional way to DL-arabinose (56%) and -xylose (54%), respectively. Aqueous silver nitrate is effective enough to hydrolyze the dichloromethyl group to the formyl to the negligible extent of epimerization[17a] (Scheme 11). Similarly,



Scheme 11

the n=2 telomers, 7a and b, derived from chloroform telogen are also converted to arabinose and xylose.[17]

On the other hand, mild hydrolysis of the telomers yields the cyclic dimers 27, which isomerize to the identical pentosulose 28 in dimeric form on the prolonged treatment under more severe acidic conditions (100-110°).[24] The pentosulose is characterized as quinoxaline derivative 29 and pentanetriol-d_2 (30) derived from



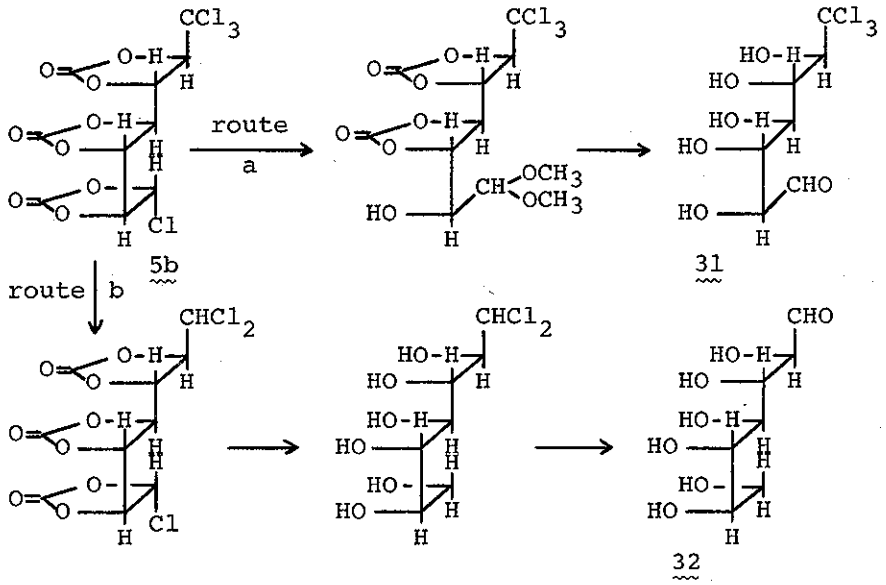
Scheme 12

o-phenylene-diamine condensation and borodeuteride reduction, respectively (Scheme 12).

Ring-opening with methanol prevents the resulting α-hydroxy-aldehyde function as the acetal from dimerizing and the successive deblocking with base and acid gives high yields (83-96%) of 5-polyhalo-5-deoxy-DL-lyxose and -xylose,[24] to which direct hydrolysis of the telomers is less satisfactory owing to the contamination with side reactions viz. epimerization, degradation etc.

Thus, three of four aldo-pentoses have been synthesized except ribose which may be prepared via cis-"syn"-cis telomer, possibly derived from ionic coordination telomerization of vinylene carbonate.

iii. heptoses from n=3 telomers: The synthetic procedure is analogous to that for the pentoses from n=2 telomers. As a typical example is presented the preparation of two kinds of heptoses (31 and 32) from the n=3 telomer 5b.[25,26] Conversion of the trichloromethyl group to the dichloromethyl followed by hydrolysis (route b) affords racemic D-glycero-D-ido-heptose (32, 30%), characterized as "β"-hexaacetate[26a] in pyranose form suggested by the nmr analysis. Alternative hydrolytic route a via acetal provides 7,7,7-trichloro-7-

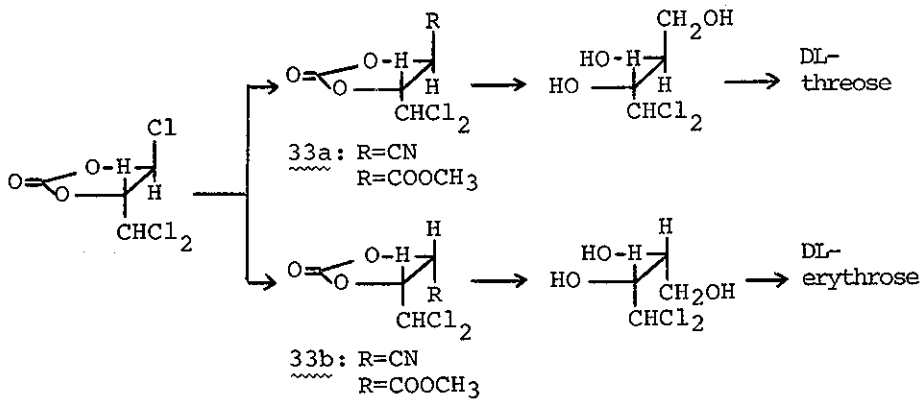


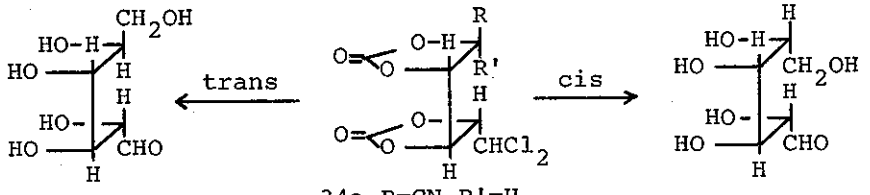
Scheme 13

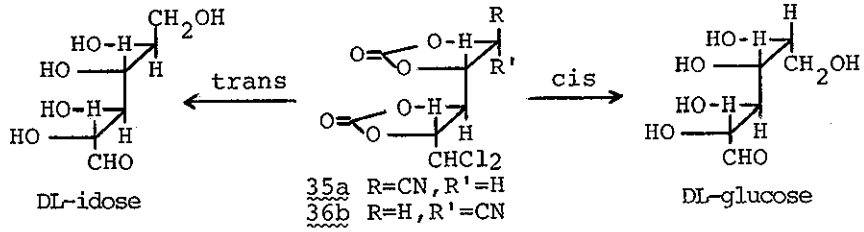
deoxy-D-glycero-L-gulo-heptose (31) in racemic form whose acetylation product is identified as the penta-O-acetyl pyranose (Scheme 13).

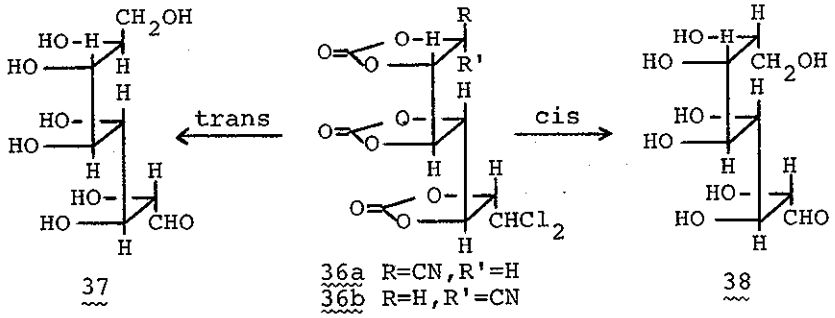
In this way, four n=3 telomers are the feasible source for the preparation of seven aldo-heptoses and derivatives, possessing D-glycero-L-galacto-, D-glycero-L-gluco-, D-glycero-D-ido-, D-glycero-L-gulo-, D-glycero-L-ido-, D-glycero-D-galacto- and D-glycero-L-manno- configurations among the sixteen possible racemic heptoses. Latter two configurations have been found in the heptose components of naturally occuring polysaccharides.[27]

iv. tetroses: Secondary halogen of the telomers at tail position is active enough to be readily replaced by various nucleophiles, alcohols, thiols, azide ions and certain carbanions.[9] Nucleophilic substitution of the telomers to the nitriles, a key-step in the synthesis, induced by phase-transfer catalysis[28] proceeds to completion


33a: R=CN
R=COOCH3
DL-threose
33b: R=CN
R=COOCH3
DL-erythrose


trans
cis
DL-galactose
34a R=CN,R'=H
34b R=H,R'=CN
DL-altrose


trans
cis
DL-idose
35a R=CN,R'=H
36b R=H,R'=CN
DL-glucose


trans
cis
37
36a R=CN,R'=H
36b R=H,R'=CN
38

Scheme 14

much more rapidly and under milder conditions than does the reaction conducted in a heterogeneous system. Cyanide displacement yields trans and cis products, 33a,b, in neatly equal amounts, which can be then converted without difficulty to DL-threose and DL-erythrose, respectively, by the conventional procedures involving esterification (CH_3OH-HCl), reduction ($NaBH_4$) and hydrolysis (H_2O-$AgNO_3$) (Scheme 14).[17]

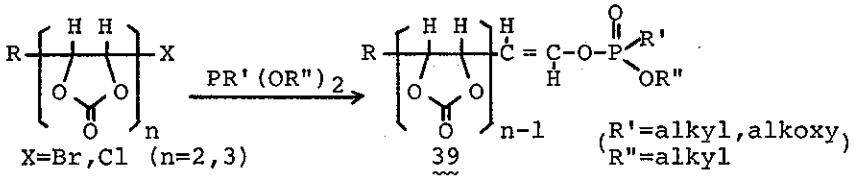
v. hexoses and octoses (Scheme 14): Similarly, four aldo-hexoses, galactose, altrose idose and glucose, are available in moderate yields from the n=2 telomers 4a and b via trans- (34a,b) and cis-nitriles (35a,b).[17]

Present method permits the preparation of D-threo-L-ido-octose (37) from the n=3 telomer 5b via trans-cyano compound (36a).[26] Identity is achieved as the octitol by gas-chromatographic comparison with the authentic sample.[19] The cis-derivative (36b) would be a synthetic source of D-erythro-D-ido-octose (38).

III-2. Phospholipid Analogues

The vinylene carbonate telomers (n=2, 3), both chloro- and bromo-compounds, smoothly react with certain tervalent phosphorus agents like phosphites and phosphonites in aprotic solvents (benzene, toluene and dioxane) to give trans enol-phosphates (39)[16] in high stereoselectivity and yields as partly mentioned above, though five-membered cyclic phosphites and the amide analogues fail to react with the telomers,[29] presumably due to the low nucleophilicity. Neither cis-isomers nor phosphonates can be formed in the sufficient amounts to be isolated. On the other hand, any products derived

from the n=1 telomers cannot be identified, in contrast with chloroethylene carbonate which gives vinyl phosphate and phosphonate in a nearly equal ratio.[30]



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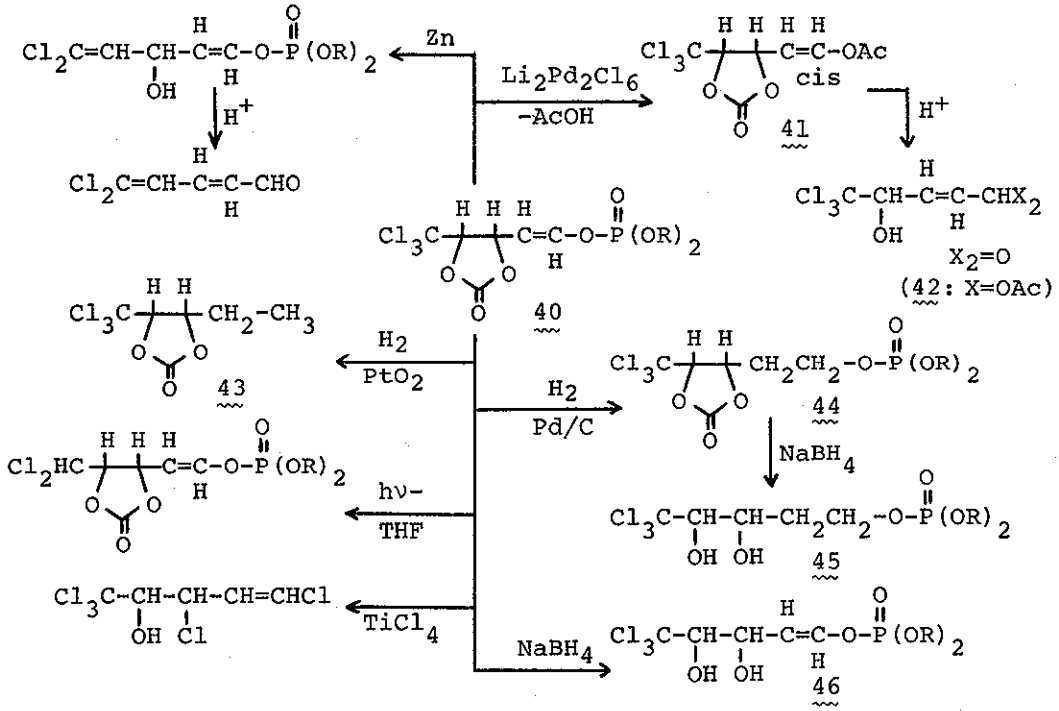
Unsaturated phosphate esters (40) thus formed may serve as versatile intermediates leading to the compounds of special interest and some typical reactions involving reductive ring-opening with zinc and photolysis in tetrahydrofuran as observed with the telomers are

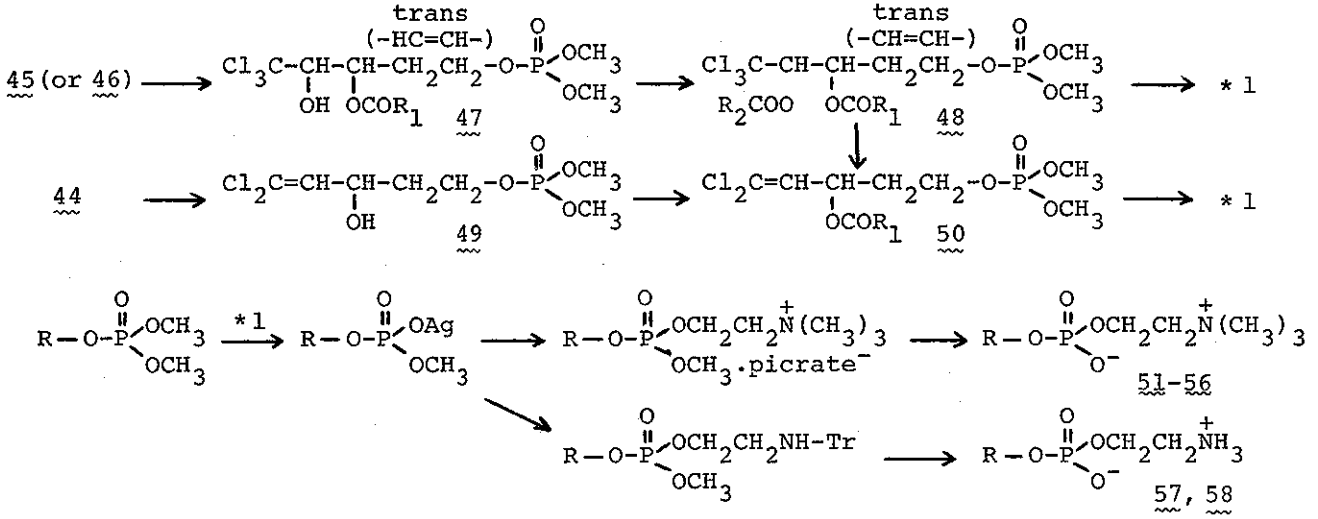


Scheme 15

shown in Scheme 15.[16] Conversion of the phosphate 40 to cis-enol acetate 41 is readily achieved by vinylic exchange reaction catalyzed by palladium (II) in acetic acid[31] and the prolonged reaction leads not to trans-vinyl acetate but to a cis and trans mixture of olefinic gem-diacetates 42 (X=OAc), while the vinyl-phosphate bond is relatively stable under the usual hydrolytic conditions to result in the exclusive formation of 46.[32] Catalytic hydrogenation with PtO_2 and Pd/C gives 43 and 44,[32] respectively. Hydrolytic cleavage of the carbonate rings of 40 and 44 affords the diols 46 and 45, which may have the synthetic potential for phospholipids and biomedical polymers (Scheme 15).

There has been an increasing need for the chemically well-defined phospholipids as the model compounds of biological and physico-chemical studies.[33] Organic synthesis is only an available source for this purpose, since it is still difficult to obtain pure phospholipids in reasonable quantities from natural sources, despite a recent improvement of isolation techniques.

Scheme 16 outlines the routes from mono- and di-hydroxy derivatives to lecithin(cholin)- and cephalin(ethanolamine)-type of unnatural phospholipids[29] which, on comparison with naturally occuring phospholipids, should aid in elucidating the relationship between the structure and the biological properties. Saturated and unsaturated diols, 45 and 46 are acylated with fatty acid chlorides to give the diacylphosphates 48, while selective mono-acylation to give 47 is achieved with acid anhydrides, presumably due to steric repulsion by a bulky trichloromethyl group and hence, an introduction



51,57: R= $Cl_3C-\overset{H}{\overset{\vdots}{C}}-\overset{H}{\overset{\blacktriangledown}{C}}-CH_2CH_2-$; $H_{35}C_{17}COO$ $OCOC_{17}H_{35}$

52: R= $Cl_3C-\overset{H}{\overset{\vdots}{C}}-\overset{H}{\overset{\blacktriangledown}{C}}-\overset{H}{C}=C-$; $H_{35}C_{17}COO$ $OCOC_{17}H_{35}$

53: R= $Cl_3C-\overset{H}{\overset{\vdots}{C}}-\overset{H}{\overset{\blacktriangledown}{C}}-CH_2CH_2-$; $H_{15}C_7COO$ $OCOC_{17}H_{35}$

54: R= $Cl_3C-\overset{H}{\overset{\vdots}{C}}-\overset{H}{\overset{\blacktriangledown}{C}}-CH_2CH_2-$; $H_{15}C_7COO$ $OCOC_7H_{15}$

55: R= $Cl_2C=CH-\underset{OCOC_{17}H_{35}}{CH}-CH_2CH_2-$

56,58: R= $\underset{H_{35}C_{17}COO}{CH_2}-\underset{OCOC_{17}H_{35}}{CH}-CH_2-$

Scheme 16

Table II.	T_1	T_2	Tc
51	64°C	206.5°C	49°C
52	61	137.5	48.5
53	<room temp.	187.5	<room temp
54	<room temp	160	<room temp
55	<room temp	189.5	<room temp
56[a]	90	231	58
57	80	140	50.5
58[b]	130	182	

a) E. Baer et al., J. Am. Chem. Soc., 78, 232 (1956); D. Chapman,"Form and Function of Phospholipids", Elsevier, 1973, p117. b) E. Baer et al., J. Am. Chem. Soc., 81, 2494 (1959).

of unlike fatty acid moieties is feasible. Mono-chain phospho-triester 50 derived from 44 via 49 is also obtainable from reductive ring-opening of 48 with zinc. Fatty acids used here are confined to stearic and caprylic acids. Tri- and tetra-hydroxy compounds from the n=3 telomers may be likewise treated to give tri- and tetra-acyl derivatives. The resulting triesters 48 and 50 can be readily converted into the corresponding phosphatidyl-cholins (51-55) and -ethanolamine (57) by well established procedures[33] as shown in the Scheme.

Utilization of the phosphonites[34] such as dialkyl (2-aminoethyl)-phosphonite in the place of phosphites may provide a route to phosphonolipids[35] containing carbon-phosphorus bond which have attracted the extensive attention for the occurence in biological materials and the inhibitory action on various phospholipases.

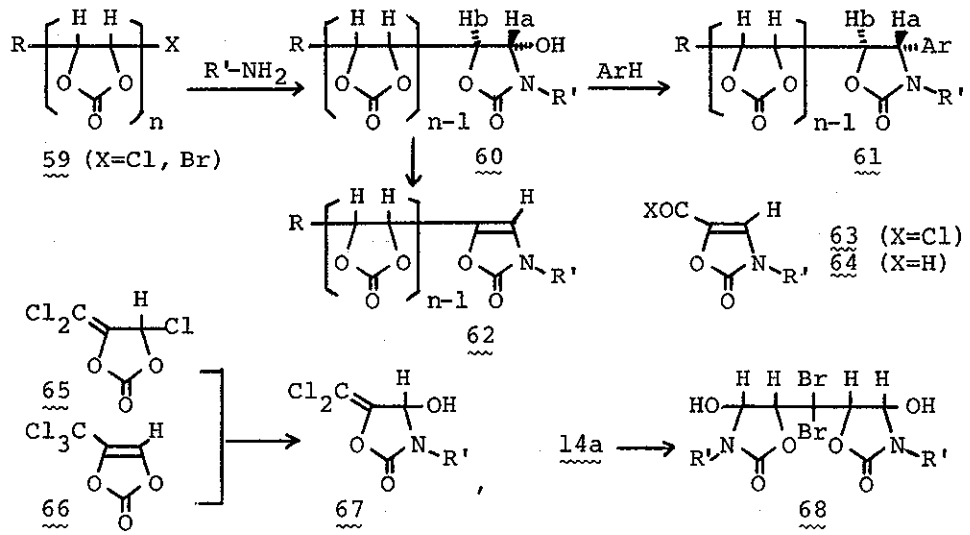
The synthetic phospholipids are able to form the thermotropic and the lyotropic liquid crystalline phases and their phase transition temperature (T_1 and T_2) as well as the Kraft point (Tc) obtained from the synthetic lipids-water binary phase-diagrams are shown together with those of natural lecithin 56 and phosphatidyl ethanolamine 58 in Table II. Interestingly, the lyposomes[29] prepared from synthetic analogues of phosphatidylcholin are able to trap a water-soluble low molecule like glucose to the nearly same extent as does natural saturated lecithin and have been discussed with regard to the insufficient barrier ability and the smaller cholesterol-fluidizing effect, probably arising from the imperfect lipid bilayers which reflect the structural difference between natural

and synthetic phospholipids. Such a barrier ability against the diffusion of water-soluble materials is one of the most important functions of membranes. Model systems of lipids would provide a valuable information on the permeability-structure relationship.[36]

III-3 2-Oxazolidones and Related Heterocycles

The 2-oxazolidones are an important class of heterocyclic compounds because of a wide variety of potential uses in biological and industrial products.[37] Here is described the smooth conversion of 4-halogeno-1,3-dioxolan-2-ones including vinylene carbonate telomers into 4-hydroxy-2-oxazolidones and related heterocycles.[38]

Treatment of 4-chloro(or bromo)-substituted 1,3-dioxolan-2-ones (59) with ammonia and primary aliphatic amines in methanol (or dimethylformamide) results in the smooth and preferential formation of crystalline trans isomers of 4-hydroxy-2-oxazolidones 60 (mostly in 70-85% yields). The conversion would involve the primary



Scheme 17

formation of the acyclic urethanes followed by facile cyclization to the five-membered heterocycles. This reaction is applied to the allylic chlorides[39] (65, 66) and compound 14a to give the expected 2-oxazolidone derivatives, 67 and 68.

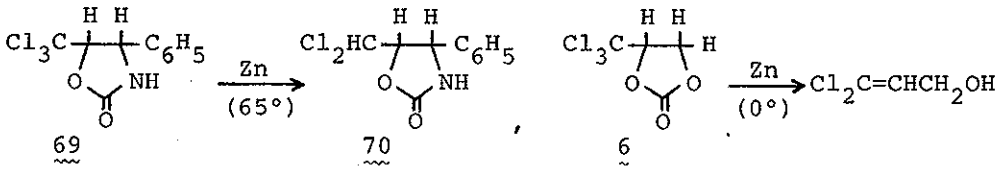
Arylation of 4-hydroxy-oxazolidone 60 (n=1) with benzene is easily performed in the presence of sulfuric acid[40] at room temperature to afford trans-4-phenyl-5-trichloromethyl-2-oxazolidone (61) stereoselectively (Table III), whose stereochemistry is based on the coupling constants (Ja,b) in the range of 3.0 to 4.5Hz.[41] On the other hand, the n=2 compound 60 yields the dehydrated 4-oxazolin-2-one derivative, 62 under the similar conditions.

Dehydration of such a heterocyclic system with trifluoroacetic acid has a precedent for the protection of primary amines including amino acids.[42] Treatment of the n=1 compounds 59 (R=CCl_3 and $CHCl_2$) with trifluoroacetic acid results in the smooth dehydration followed by simultaneous hydrolysis of the allylic trihalide (probably formed) to give the acid chloride 63 and the aldehyde 64, respectively, which are useful for the preparation of a variety of 5-substituted 4-oxazolin-2-ones (Scheme 17).

Table III. Conversion to 2-Oxazolidones and Related Compounds[24]

R	R'	60	61	62
H	benzyl (n=1)	85 %		20 %
CCl_3	H (n=1)	74	86 %	96 (63)
CCl_3	methyl (n=1)	76		98 (63)
CCl_3	benzyl (n=1)	33	81	95 (63)
CCl_3	cyclohexyl (n=1)	72	74	96 (63)
$CHCl_2$	benzyl (n=1)	20		96 (64)
CCl_3	cyclohexyl (n=2)	70		97

Contrary to the quite facile and complete ring-opening of 4-trichloromethyl-1,3-dioxolan-2-one (6) to the ally alcohol by the familiar reductive cleavage of β-polyhaloethoxy group,[12,43] the 2-oxazolidone ring is stable even when 69 is treated with zinc in boiling methanol, resulting in the exclusive reduction to the dichloromethyl derivative 70.[38]



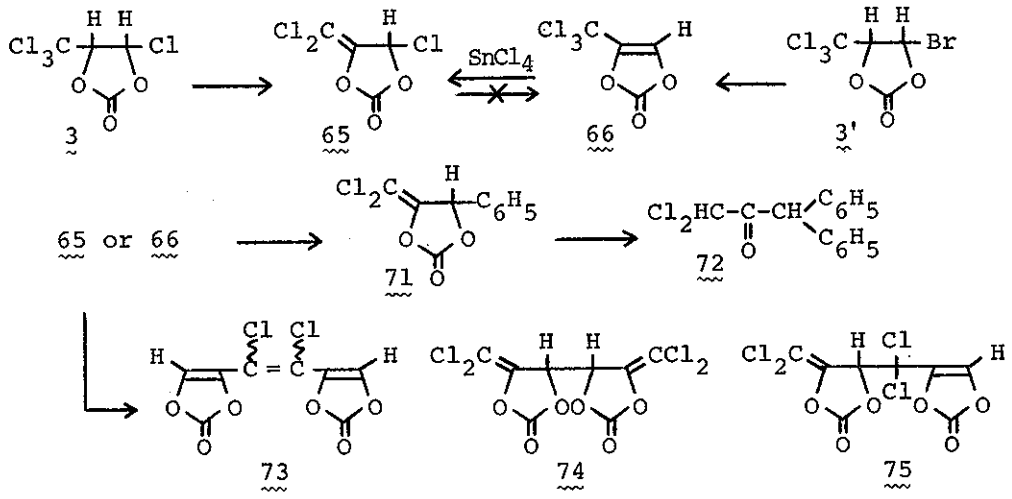
IV Miscellaneous Reactions

IV-1. Dehydrohalogenation

It is desirable to develop the widely applicable synthetic utilization of the n=1 telomers, since they are obtainable exclusively or at least in an excellent yield by easy control of the telomerization conditions. Allylic halides is an intriguing system due to high reactivity, particularly toward organo-metallic agents, and may be a compound of choice.

Dehydrohalogenation with triethylamine gives a high yield (60-80%) of allylic trihalides, 65 or 66, depending on the starting telomers[39] and treatment with pyridine affords a pyridinium adduct quantitatively. In the presence of Lewis acids, 66 isomerizes to 65 exclusively and the reverse is not observed. The Friedel-Craft and the coupling reactions which do not take place at the telomer level, are shown as the typical in Scheme 18.

Diaryl compound 72 arises from the reaction of 65 or 66 with



Scheme 18

benzene by use of $AlCl_3$ or $FeCl_3$ as a catalyst, while the use of iron pentacarbonyl or diiron enneacarbonyl gives mono-phenylated compound 71 as a major product.[44] This reaction may be of interest as a method permitting the introduction of functionalized C_3-unit into the aromatic molecule.

Coupling reaction with low valence metallic agents such as Ni(0), Fe(0), Cu(0) etc. in dimethylformamide or tetrahydrofuran affords the olefinic C_6-compounds 73-75 which may play a role in ketose and cyclitol preparation.

IV-2. Dehalogenative Reduction

Only few among the reported methods[23,45] are mild and selective enough to convert the trihalomethyl groups to the di- and mono-halomethyls in the labile compounds like the present telomers. Two promising procedures involving the reaction with nickel carbonyl[12] and the photolysis[20] in tetrahydrofuran have been developed for such

Table IV. Conversion to Lower Halides. $R-\overset{X}{\underset{X(H)}{C}}-X \longrightarrow R-\overset{X}{\underset{X(H)}{C}}-H$

Compound (X)	Method[a]	Mole ratio[b] (Concent.)[c]	Time	Yield[d]	Reference
3 (Cl)	A	2	48 hr	53 %	12)
	B	(20)	3	76	20)
4a (Cl)	B	(3)	5	79	17)
5b (Cl)	B	(3)	3	84	18),24)
6 (Cl)	A	2	24	38 (55)	12)
	B	(10)	7	84	17)
7b (Cl)	B	(3)	5	79	17)
12b (Br)	A	50	16	42	8),12)
13	A	3	5	69	12)
14a (Br)	A	6	3	71	12)
	B	(1)	7	71	13)
15 (Br)	A	2.5	2.5	63	17)
($R=COOCH_3$)	B	(68)	4.5	58	17)
19b (Br)	B	(1)	7	89	13)
40 (Cl)	B	(6.5)	5	80	16)
DDT (Cl)	A	2	48	86	12)
Ph_2CHCBr_3	A	2	5	86	12)
i (Cl)	B	12	11	78	20)
ii (Br)	B	11	8	69	20)
iii (Br)	B	(2)	6	24 (13)	20)
$PhCCl_3$	A	2	4	36 (50)	12)
	B	(12)	4	40 (7)	20)

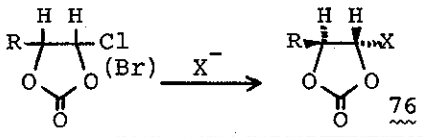
a) A: $Ni(CO)_4$-THF, B: UV-irradiation in THF. b) $Ni(CO)_4$/halide. c) 10^{-2}M/l. d) Isolated yield. Recovery of starting material in parentheses (%). i: 1,1,1,3-Tetrachlorooctane. ii: 1,1,1,3-Tetrabromononane. iii: 7,7-Dibromonorcarane.

a stepwise conversion to lower halides. Results obtained so far show a wide applicability of the methods (Table IV). For an acid-sensitive compounds, the former method which proceeds under neutral conditions, may take advantage over the photolytic reduction which accompanies the substantial amounts of hydrogen halides.

Both reactions would proceed in a radical mechanism involving a homolytic cleavage of carbon-halogen bond followed by the abstraction of hydrogen from the tetrahydrofuran, the most effective solvent examined.

IV-3. Nucleophilic Substitution

Secondary halogen on the carbonate ring of the telomers may be smoothly displaced by alkoxy, acyloxy, alkylthio and azide groups under the Koenigs-Knorr[46] or the basic conditions to give trans-products 76 exclusively. A carbon unit may be introduced into the 4-halo-1,3-dioxolan-2-one system in moderate yields by the reactions with sodium salts of hydrogen cyanide or acetamidomalonate, while the introduction of simple alkyl, alkenyl and alkyne groups has been far less satisfactory to date (below 20% yield at best) by the use of various metallic reagents involving "cuprate" complexes.[47] Typical examples observed with n=1 telomer(s) are shown below.



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X	: OCH_3	OAc	SEt	N_3	CN	$C(COOEt)_2$ NHAc	n-Bu	C≡C-Ph	$^{+}$N⟨⟩
Yield(%):	88	71	58	60	72[a]	52	6	16	~100

a) including cis-isomer

In conclusion, the present type of telomerization has a potential for synthesis of a wide variety of poly-functional compounds as demonstrated by some synthetic applications and the reactivities of the telomers surveyed here.

Next challenging target in the related field may be a development of new catalytic systems for coordination telomerization of vinylene carbonate,[48] in which higher stereoselectivity with regard to "syn" and "anti" as well as cis and trans, may be hopefully anticipated, since there has appeared "only one" precedent, in the above sence, of highly stereo-regulated polymerization of cyclobutene using the Ziegler-Natta catalysts.[49]

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