Translated from *Uspekhi Khimii* **60** 2020–2046 (1991) U.D.C. 547.421

# *gem*-Polyols — a unique class of compound

**Yu M Shapiro**
The Polytechnic Institute, Krasnodar

ABSTRACT. The formation and conversions of *gem*-polyols have been examined together with their chemical and physical properties.

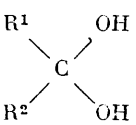
The bibliography contains 123 references.

## Contents

I. Introduction 1035
II. The reality of 'hypothetical' compounds 1036
III. *gem*-Polyols as members of the *gem*-polyhydroxide family 1046

## I. Introduction

Polyalcohols with a geminal structure (I), i.e. *gem*-polyols, are an ill-defined class of organic compound.

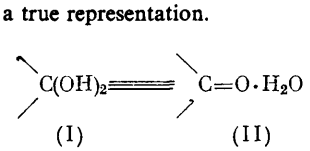


(I)

where $R^1$ and $R^2$ = OH or another group of atoms or a specific atom.

In his time, A M Butlerov was puzzled by the fact that "...methyl[ene] glycol was not only unknown but that its existence seemed unlikely: it was not obtained in reactions where its formation might have been anticipated. At present, theory cannot adequately explain this phenomenon..."[1] Although, today, a large number of stable compounds with structure (I) are known, including methylene glycol as the primary form of formaldehyde in aqueous solution,[2] *gem*-polyols more usually play a secondary, incidental role in chemistry as the hydrated form of carbonyl compounds. In the *Universal Decimal Classification* of recent years,[3] it is stated under the entry 547.421.2 that structure (I) represents 'Hypothetical geminal glycols'. In a standard text-book,[4] it is said that on formation of *gem*-diols they are immediately converted into the corresponding aldehyde or ketone.

The fact that the *gem*-polyol structure (I) has not been recognised is evident in nomenclature and formulae which chemists have adopted. Even specialists in this field have referred to such as hydrated carbonyl compounds with structure (II), which clearly is far from a true representation.



(I) (II)

Thus, doubt on the authenticity of (I) has existed since the early days of organic chemistry and remains today. This is, in part, because of their unique properties, which are quite different from those of simple alcohols, and, in part, because little research has been carried out in this field. The chemistry of their formation and subsequent conversions cannot be generalised. Rather, it is dependent on the particular structure of the molecule, the medium, and other factors. Specific information on the nature of *gem*-polyols is still needed in all areas.

In spite of the fact that new data on the properties of (I) are currently being reported in the literature, reviews on this subject are sparse. From the period 1966 to date, the key cited reference is still that on the reversible hydration of aliphatic aldehydes[5] (Russian version see Ref. 6). Monographs have been devoted to the important analytical reagent, ninhydrin, and its analogues, which are stable *gem*-diols.[7,8] Furans with a *gem*-polyol group, and related compounds, have been discussed as part of a review.[9]

Derivatives of (I), especially acetals[10] and orthoesters,[11,12] have been reviewed much more. However, such compounds, which today are readily available, are not normally prepared from *gem*-polyols and therefore have no direct bearing on the theme of the present review.

The study of the chemistry of *gem*-polyols is important for the understanding of a whole range of reactions, certain of which pertain to quite unrelated aspects of organic and inorganic chemistry. These include the hydration of carbonyl-containing compounds and oxides, the interconversion of pyro-, meta- and ortho-acids, the hydrolysis of esters, the condensation of carbonyl-containing compounds, catalysis and isotopic exchange, hydride transfer and other redox conversions of polyhydroxides, etc. Significantly, *gem*-polyols or their derivatives are invariably cited as intermediates in any mechanistic analysis of the above reactions.[13–20] However, in most instances, the representation of *gem*-polyol intermediates is purely symbolic and does not imply the existence of molecules of structure (I) as real compounds.

The present review is devoted strictly to *gem*-polyols and reactions which are specific to them. From the accumulated experimental data, it has been possible to distinguish and consider (I) as a distinct class quite apart from carbonyl-containing compounds.

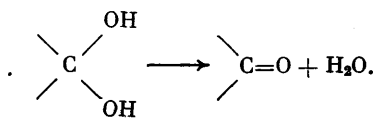
For convenience, *gem*-polyols can be subdivided into three groups: 1) stable, normally crystalline compounds; 2) less stable compounds which exist only in solution; and 3) very unstable intermediates. The first two groups refer essentially to *gem*-diols as a distinct class, while the third embraces all forms of *gem*-polyol. In certain instances, the salt form is more stable than the neutral molecule.

A whole range of modern techniques has been utilised for structural analysis of (I) and for the elucidation of the nature of the species in solution. A number of these have been discussed before.[5,6] They include UV-, IR-, and NMR-spectroscopy, circular dichroism,

polarograph, isotopic exchange, and chemical analysis. Each of these methods has its limitations, so that alternative analyses are always required. Thus, polarographic data on the hydration of aldehydes has, in certain instances, been disputed because of the inherent speed of the methodology, while others argue the obvious benefits of being able to regulate the pH and voltage accurately.[21]

## II. The reality of 'hypothetical' compounds

Doubt on the authenticity of geminal polyols is basically groundless. In reality, these compounds are in equilibrium with the corresponding carbonyl compounds and water:



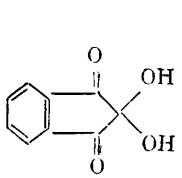
Normally, dehydration is facile, although in certain instances difficulty has been encountered. References in the literature to stable *gem*-diols first appeared in 1910 with reports on the synthesis of ninhydrin,[7] in which one of its three keto groups is hydrated with ease. Today, the list of such compounds is significant, and many authors have studied the factors which control the equilibrium between the *gem*-polyol (*gem*-diol in most instances) and carbonyl form. One elementary fact has been established: electron-accepting groups adjacent to the *gem*-diol group tend to stabilise, and electron-donating groups destabilise, the function. However, this is a complex issue since many other factors have to be considered. The requirements of listing all known *gem*-polyols (I) is clear, as also is the examination of their behaviour in different media and the results of structural analyses, etc.

### 1. Crystalline *gem*-diols

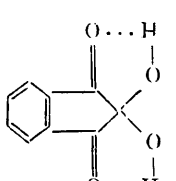
For convenience, these compounds have been subdivided into the following categories: 1) products obtained by hydration of aliphatic α-halogeno-ketones and -aldehydes, 2) aldehydo- or keto-hydrates of a number of α-aldehydo- and α-keto-acids, polyketones and α-keto-aldehydes, 3) hydrates of pyridylcarbonyl compounds, 4) conjugated cyclic ketone hydrates, and 5) *gem*-diols stabilised by intramolecular hydrogen bonds. The latter is evidently a factor to consider with all *gem*-diols.

#### a) Carbonyl-containing dihydroxymethylenes

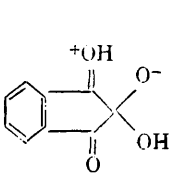
Ninhydrin is a well-known reagent for detection of amino groups (especially amino-acids). It exists in the very stable *gem*-diol form (III), both in the crystalline state and in solution.[7,8] Rukhman[7] was first to study the stability of (III), and proposed that either hydrogen bonding, as in (IV), was responsible or that stabilisation was gained by the formation of a zwitter ion (V).



(III)



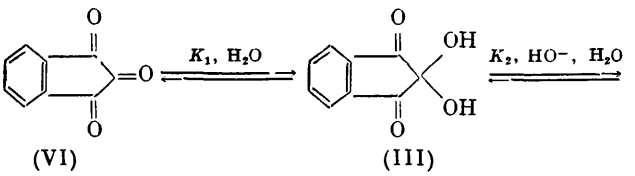
(IV)



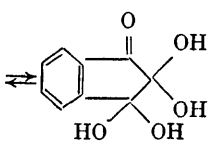
(V)

The formation of (III) proceeds readily even on dissolving 1,2,3-indantrione (VI) in water. A second carbonyl group is hydrated under base catalysis.[22] It is proposed that the anionic form (VIII) of ninhydrin is involved in the formation of the dihydration (VII). The relative amounts of the three forms (III, VI and VII) have been calculated as follows:

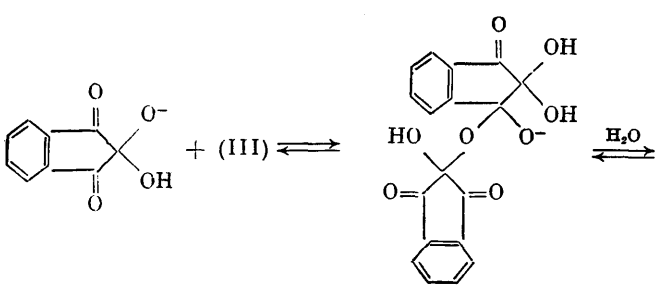
$$K_1 = \frac{[III]}{[VI]} = 2.9 \cdot 10^3; \quad K_2 = \frac{[VII]}{[III]} = 0{,}31 \pm 0.04;$$



(VI) (III)



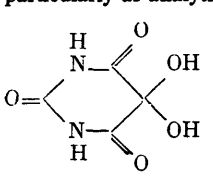
(VII)



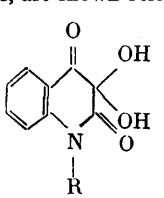
(VIII)

(VII) + (VIII).

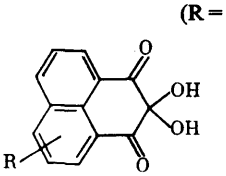
The 'ninhydrin phenomenon' pioneered research into the synthesis of other cyclic polyketones capable of forming *gem*-diols on hydration.[8] Certain of these compounds which have proved useful, particularly as analytical reagents, are shown below.



Alloxan



Quinisatin and its derivatives (R = H, $CH_3$, Ph)

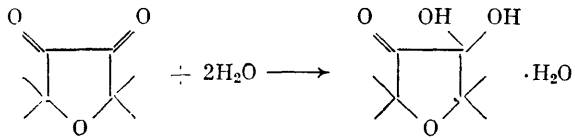


Perinaphthindantrione hydrate and its nitro derivative (R = H, $NO_2$)

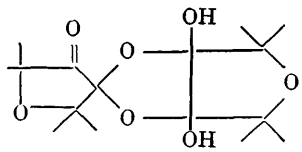
Multi-step syntheses of oxirene [sic (Ed. of Translation)] and phenalene *gem*-diols have been reported.[23] The hydration of cyclic 1,2,3-tricarbonyl compounds has also been studied[24,25] and reviewed over a long period of time in monographs.[7,8]

Dehydration normally requires harsh conditions: distillation *in vacuo* or heating in oleum in methylene chloride.[25] For reactions proceeding via dehydration of *gem*-diols, syntheses have also been carried out in concentrated sulphuric acid.

Studies of the hydrated forms of 2,2,5,5-tetramethylfuran-3(2*H*)-4(5*H*)-dione have shown that two structures exist in the crystalline state.[26,27] One incorporates 2 molecules of water for each molecule of the diketone and the other 0.5 molecules of water. In the 'dihydrate' structure, one of the two molecules of water is involved with *gem*-diol formation while the other is associated as a crystal hydrate:



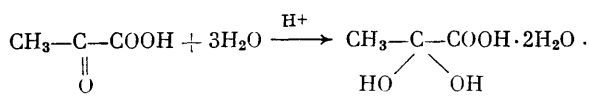
The authors propose a hydrated dimeric structure for the other crystalline form:



Significantly, the non-hydrated form of this diketone is coloured, while the hydrate is colourless. This is unusual and thought to be a consequence of strain in the non-hydrated furan skeleton and the presence of hyperconjugation with the keto-groups. Neither is possible in the *gem*-diol form.

There is reference to a large number of acyclic analogues, formed by hydration of ketones or aldehydes functionalised in the α-position by the carbonyl group of another aldehyde or ketone function or of a carboxyl function or derivatives thereof (e. g. an ester group).

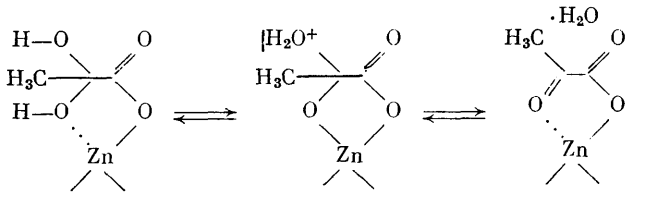
Much research has been devoted to pyruvic acid since this is important biologically. It has been shown that in the crystalline form the hydrate incorporates three molecules, only one being involved with *gem*-diol formation.[28] This hydration is catalysed by protic acids:



For the hydration of pyruvic acid by metalloenzyme complexes [sic (Ed. of Translation)],[29] the order of catalytic activity is as follows:

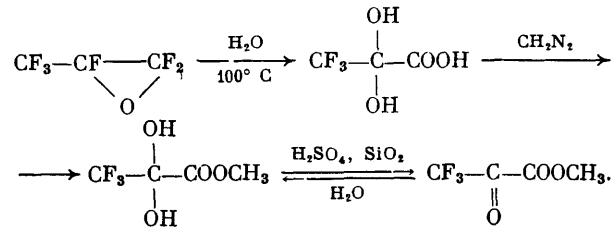
$$Cu^{2+}>Zn^{2+}>Ni^{2+}>Co^{2+}>Cd^{2+}>Mn^{2+}\ .$$

This order is in keeping with the ability of the metal to form a chelate complex with pyruvic acid. For the zinc-catalysed hydration in the presence of carbonic anhydrase, the following scheme has been proposed:

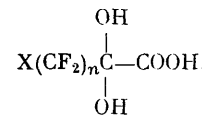


The hydration of pyruvic acid esters has also been reported.[30]

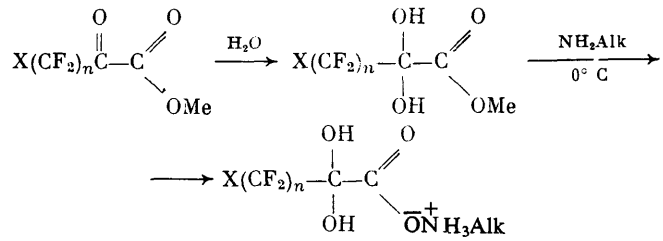
Hydration of halogenated pyruvic acids to the corresponding *gem*-diols is noticeably enhanced. Thus, hydrolysis of perfluoropropylene oxide affords directly trifluoropyruvic acid in the hydrate form (m.p. 124–126 °C; b.p. 156–158 °C).[31] Subsequent treatment with diazomethane gives the corresponding methyl ester. The resulting *gem*-diol dehydrates on heating in sulphuric acid containing silica gel to give methyl trifluoropyruvate, which readily reverts to the *gem*-diol on addition of water.



This research has been extended to the preparation of related fluorinated α,α-dihydroxycarboxylic acids,[32,33] their esters and various alkylamine salts.[34]



X = H, F, $n$ = 1–4.



Structural analyses have been carried out by IR-spectroscopy ($\nu_{OH}$ = 3300–3370 $cm^{-1}$) and NMR-spectroscopy ($^1H$ and $^{19}F$).

**b) Halogenated dihydroxymethylenes**

In a review of their own work on polarographic and spectroscopic (UV) studies,[35] the authors pointed out the correlation between the stability of α-halogenated aldehyde hydrates and the number of halogen atoms. It was also noted that chlorinated hydrates are more stable than bromo derivatives. On the other hand, the stability of the hydrates decreases with increase in length of the alkyl chain. Many systematic analyses published in recent years[5,6] have shown that the stability of halogenated *gem*-diols obtained by hydration of aliphatic fluoro-, chloro- and bromo-aldehydes and -ketones decreases in the order F > Cl > Br. Trihalogeno derivatives are crystalline compounds while most other halogenated *gem*-diols exist only in solution. Chloral hydrate, which has a large number of practical applications, is clearly the best known of these halogenated *gem*-diols. NMR-spectroscopy and circular dichroism both confirm its structure as $CCl_3CH(OH)_2$ rather than the free hydrate, $CCl_3CH{=}O.H_2O$.[6]

It is interesting here to note one of the methods of preparing chloral from chloral hydrate.[36] Commercial 'chloral hydrate', comprising 73.5% chloral hydrate, 6.2% chloral and a mixture of acetals and hemiacetals, is heated for 20 min at 110–120 °C at 1.5–2 atm under nitrogen. The upper layer of the resulting product mixture contains 99% chloral.

Studies have shown that, even with polyhalogenated derivatives, the equilibrium between *gem*-diol and carbonyl form is markedly dependent on the medium.[37,38] $^1H$ NMR spectroscopy has indicated

that chloral hydrate and related compounds spontaneously dehydrate in non-polar media (Table 1). An increase in the polarity, which has been equated with the basicity (B),[38] leads to a shift in the equilibrium in favour of the *gem*-diol form:

$$\underset{\text{(A)}}{CCl_3—CH(OH)_2} \rightleftharpoons \underset{\text{(B)}}{CCl_3—CH=O} + H_2O.$$

From the data in Table 1, the stability constants ($K$) for the *gem*-diols in nitromethane have been calculated from the proportion of carbonyl form in the mixture.

$$K = A/B.$$

Thus, for chloral hydrate, bromal hydrate and α,α-dichlorobutyral hydrate, $K$ = 4.9, 0.45 and 0.89, respectively.

**Table 1. The proportion of the aldehyde form (%) of α-halogenoaldehydes in different solvents.[37]**

| Solvent | Compound | | | B* |
|---|---|---|---|---|
| | $CCl_3CH=O$ | $CBr_3CH=O$ | $C_3H_7CCl_2CH=O$ | |
| $CCl_4$ | 82 | 100 | 100 | 0 |
| $CHCl_3$ | 60 | 67 | 88 | 4 |
| $CH_2Cl_2$ | 35 | 69 | 100 | 23 |
| $ClCH_2-CH_2Cl$ | 34 | 66 | 79 | 40 |
| $C_6H_6$ | 60 | 100 | 100 | 48 |
| $CH_3-NO_2$ | 17 | 69 | 53 | 63 |
| $CH_3-CN$ | 0 | 20 | 41 | 160 |
| $D_2O$ | 0 | 0 | 0 | 156 |
| $CD_3OD$ | 0 | 0 | 0 | 218 |
| $(CD_3)_2C=O$ | 0 | 12 | 29 | 224 |
| $(CD_3)_2S=O$ | 0 | 2 | 7 | 312 |

* B — the relative value of solvent basicity.

A kinetic study of the hydration of trichloroacetaldehyde in aqueous dioxane[39] has shown that four molecules of water may be associated with the aldehyde in the form of a cyclic complex. IR-spectroscopy and circular dichroism spectroscopy indicate that the hydrates of hexachloroacetone, other halogenated acetones, and chloral form adducts with dioxane, cyclohexanone, cyclopentanone, dimethyl sulphoxide, and other bases.[40] The hydrate of hexachloroacetone also incorporates four molecules of water.

There is a reference[41] to the preparation of chloral hydrate by chlorination of ethanol in water under irradiation:

$$CH_3CH_2OH + 4Cl_2 + H_2O \rightarrow CCl_3CH(OH)_2 + 5HCl.$$

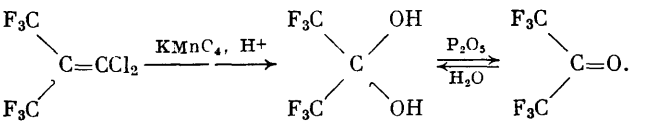
The product, in hydrate form, is distilled from the reaction mixture (b.p. 97.5 °C, m.p. 53 °C) and dehydrated by heating with concentrated sulphuric acid.

Aldehydes with a trifluoromethyl group in any location other than the α-position do not form crystalline hydrates.[42] They may be prepared by routine oxidation of the corresponding primary alcohols.

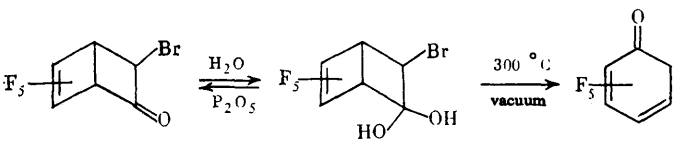
$$CF_3CH_2CH_2OH \xrightarrow{K_2Cr_2O_7,\ H_2SO_4} CF_3CH_2CH=O.$$

Trifluoroacetaldehyde cannot be prepared by this route. However, there is an indirect synthesis based on the conversion of trifluoroacetamide to the corresponding nitrile, followed by treatment with ethereal $LiAlH_4$ and concentrated HCl. The crystal hydrate of fluoral is dehydrated over $P_2O_5$.

Hexafluoroacetone was prepared for the first time in 1941 by direct fluorination of acetone in the gas phase over a copper gauze (m.p. −129 °C, b.p. −28 °C).[43] A more convenient method[44] involves oxidation of 1,1-dichloro-2,2-bis(trifluoromethyl)ethene in aqueous media, followed by cautious addition of the resulting hydrate (b.p. 57 °C at 93 mmHg) to $P_2O_5$:



The involvement of a hydrate form in the chemical conversion of a complex fluorinated ketone has also been reported:[45]

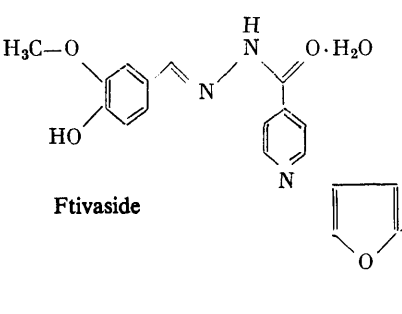


$\nu_{OH}$ 3440 см$^{-1}$
m.p. 55–57 °C

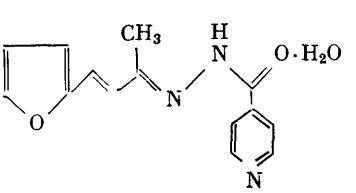
**c) Pyridyl-substituted dihydroxymethylene compounds**

Pyridinecarboxaldehydes, in particular 2-pyridyl and 4-pyridyl derivatives, are readily converted to crystalline hydrates.[46–49] Thus, 4-pyridinecarboxaldehyde hydrate is obtained by mixing the aldehyde itself with a 15-fold excess of water at 10–15 °C.[46] The resulting hydrate is a white, crystalline powder, m.p. 64–68.5 °C. Quinoline analogues have similar properties.[49] On the other hand, benzaldehydes and other compounds[50] are only hydrated in solution, provided that there is an electron-accepting substituent in the molecule.

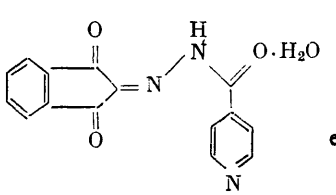
According to one reference book,[51] and elsewhere,[52] it is also reported that tuberculostatic isonicotinoylhydrazones also form crystal hydrates:



Ftivaside

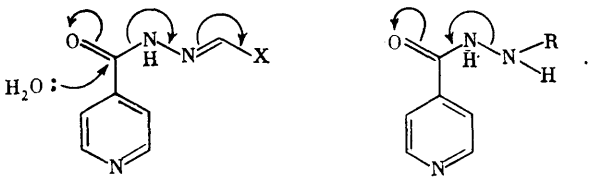


Larusan



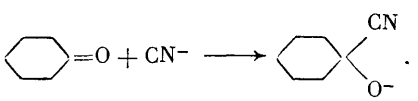
etc.

The precise nature of the hydrate form has not yet been established.[52] Significantly, isonicotinic acid hydrazides do not form hydrates. Thus, it can be assumed that hydration is primarily determined by the electron-accepting effect of the hydrazone residue on the carbon atom of the carbonyl group. Such stabilisation is absent in the free hydrazide:

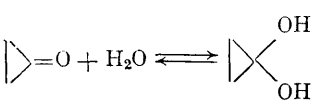


**d) Dihydroxymethylene derivatives of strained ring systems**

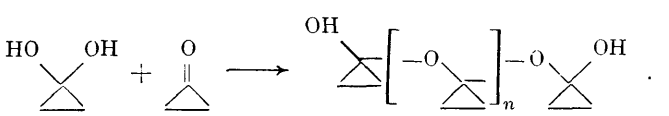
For cyclic systems, the interconversion between planar ($sp^2$) carbonyl structure and tetrahedral ($sp^3$) *gem*-diol form is associated with a structural modification of the whole molecule. In such compounds, neither form is especially favoured by neighbouring substituents. Strain in the ring system essentially determines the course of such (de)hydration, as well as other related reactions. Thus, while cyclohexanone interacts smoothly with cyanide ion (see below) and semicarbazide, there is no such reaction with cyclopentanone and cyclobutanone.[53]



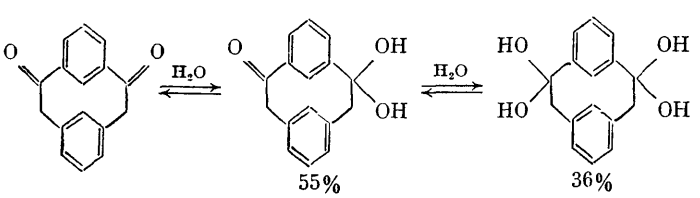
Cyclopropanone is readily hydrated to give the stable 1,1-dihydroxycyclopropane[53–56] (m. p. 82–84 °C).



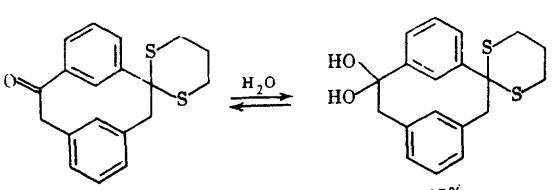
Ring strain also activates the hydroxyl groups of the *gem*-diol, leading to the formation of polymers:



Ketone derivatives of [2,2]metacyclophane are also readily hydrated to give crystalline *gem*-diols:[57]



55% 36%

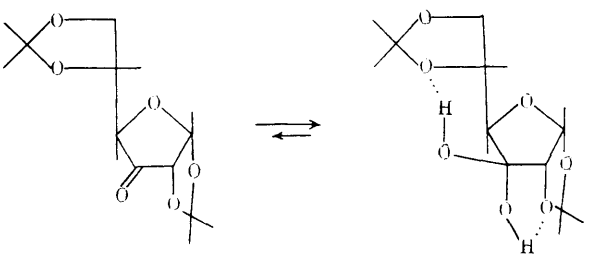


45%

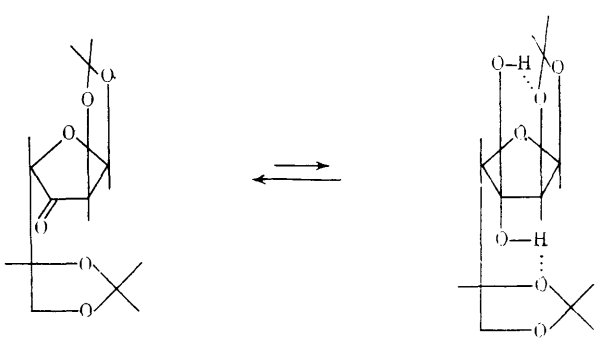
The fact that ring strain may be responsible for the readiness to form hydrates, as in the cyclic compounds shown above, may in part explain why aromatic compounds, such as benzaldehyde and acetophenone, do not exist in the hydrate form.[9]

Ring strain and the influence of electro-accepting groups within the same molecule may contribute together in stabilising the *gem*-diol form. This clearly explains the high stability of ninhydrin[7,8] as well as the facile hydration of tetrahydrofuran-3,4-diones[26,27] and fluorinated bicyclo[2.2.0]hexenones,[45] which change colour on hydrate formation.

There is also the possibility of stabilisation of the *gem*-diol structure in a tetrahydrofuran system by both ring strain and hydrogen bonding with adjacent groups. This is evident in isomeric 1,2:5,6-di-*O*-isopropylidene-*D*-hexafuranoses having a keto group in the 3-position.[58–60]



m.p. 109–111 °C



Studies have shown that *gem*-diol intermediates play an important role in the interconversion of these isomers, as well as in various syntheses based on these compounds.

The data presented in this section support the view that *gem*-diols are a genuine class of compound, contrary to established belief. However, the list of known *gem*-diols is not great, so that it is not yet possible to make theoretical generalisations. The number of less stable *gem*-polyols is significantly greater, but, in contrast to those mentioned above, they exist only in solution.

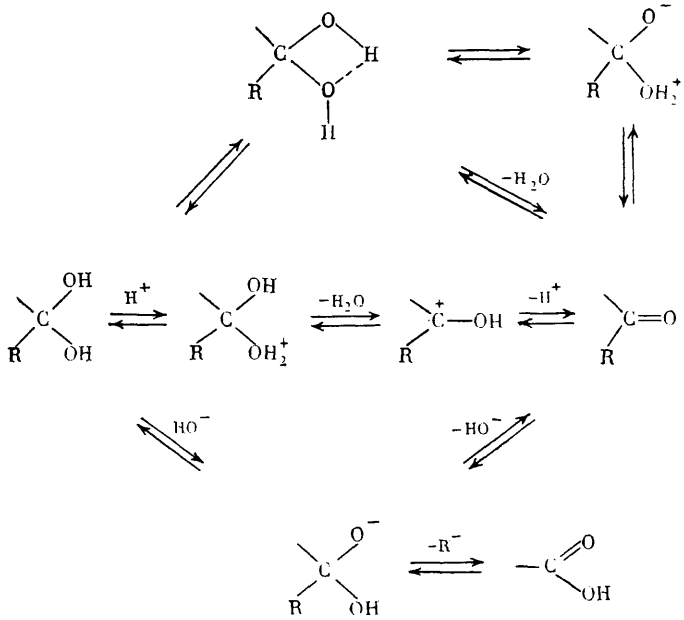
## 2. *gem*-Polyols in solution

The formation of *gem*-diols (I) can take place in water, or media containing water, by a number of routes: by hydrolysis of halogenoalkanes, hydration of carbonyl compounds, carboxamides, etc., and by exchange of various functions by hydroxyl groups. *gem*-Diols may also be converted into other functional groups in such aqueous media. Studies of the products formed by certain reactions of carbonyl and other compounds[13–20] often indicate that *gem*-diols are short-lived intermediates. However, it may not always be possible to trap them by established techniques.

**a) Stability and acid-base properties of *gem*-diols**

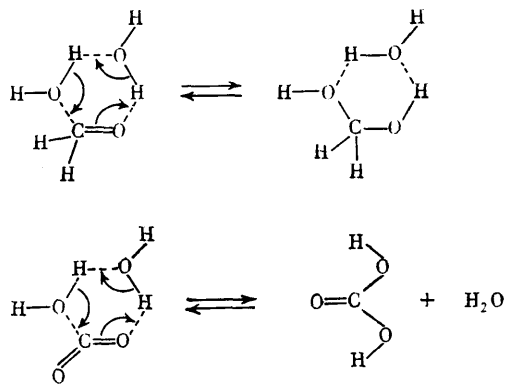
The recognition[5,6] that *gem*-diols are formed reversibly on hydration of aldehydes and ketones has had a profound effect on subsequent studies in this area and has been generally accepted by those who have undertaken theoretical analyses of the chemistry of carbonyl compounds.[13–20,47] Scheme 1 outlines the three possible routes for the formation and cleavage of *gem*-diols: in neutral media and under basic or acidic catalysis. However, conditions may be such that a clear distinction between these pathways cannot always be made.

Scheme 1



R = H, Alk, Ar, OH, $NH_2$ etc.

By considering the carbonyl form as starting material, only one process is involved: nucleophilic addition of oxygen at the carbon atom of the carbonyl group. Acid catalysis increases the developing positive charge at this carbon atom, thereby facilitating nucleophilic attack, in the same manner as a Lewis acid. Under basic catalysis, nucleophilic attack proceeds with direct participation of an alkoxide anion. It has been shown[61,62] that in neutral media, molecules of water are associated in a cyclic complex, thereby polarising the carbonyl group in the same manner as an acid catalyst.

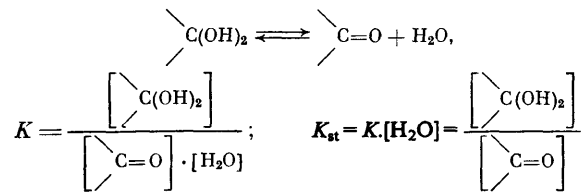


The above-described mechanism of carbonyl group hydration is essentially the same for aldehydes and ketones of various type as well as for carbon dioxide. All the possible catalytic pathways for hydration of the latter have been discussed in a review article.[63]

The pathways outlined in Scheme 1 have also been examined from the side of the *gem*-diol. In this case, the catalytic and 'non-catalytic' routes are more distinct. The instability of *gem*-diols in water at pH 7 is thought to arise by self-protonation.[64] Acid catalysis is effectively the same since the initially formed species is an unstable hydroxonium salt. Under basic catalysis *gem*-diols may often become more stabilised in such a way that subsequent conversions may be determined by secondary reactions, for example by transfer of hydride ion[18] or heterolytic cleavage of a carbon–carbon bond.[19]

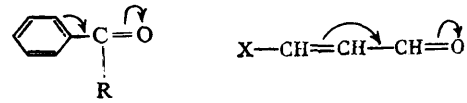
It is clear from the above discussion that the aspect of *gem*-diol stability is a very complex one. In aqueous media, *gem*-diols may be highly stable but impossible to isolate as such. On the other hand crystalline compounds may undergo a variety of conversions on dissolution. *gem*-Diols may not always be cleaved on acid catalysis. In studying the conditions for hydration of pyruvic acid it has been found that the rate of hydration increases in the presence of an excess of propionic acid.[65] The latter thus serves as a mild acid catalyst for the conversion of carbonyl compounds to *gem*-diols.

In order to compare the stability of *gem*-diols, the stability constants, $K_{ST}$ where $K_{ST} = 1/K_d$), for a number of compounds have been listed in Table 2.



The data presented in Table 2, selected from known sources, have in the main been evaluated from the constants $K_d$ (or $K_h$) or determined from the reported concentrations of the carbonyl and *gem*-diol forms. The value of $K_{ST}$ in these examples is a more meaningful indication of the stability of the *gem*-diol, while $K_d$ ($K_h$) has been used for an indication of the relative amount of the carbonyl (non-hydrated) form.

For aliphatic compounds it has recently been established that aldehydes are hydrated more easily than ketones. The stability of *gem*-diols increases as electron-accepting groups are introduced into the molecule and decreases on introducing electron-donating substituents. The ready hydration of α-ketocarboxylic acids and their salts is an obvious example to support this point. For aromatic and α,β-unsaturated aldehydes and ketones, there is less likelihood of forming *gem*-diols, even in neutral aqueous media, since the electron deficit of the carbonyl carbon is effectively neutralised by conjugation with the π-electron system.[5,6]



At the same time, dihydroxymethylene derivatives of [2,2]metacyclophane in aqueous solution have quite a high stability, although they can be regarded as analogues of hydrated aromatic ketones.[57] Acetone hydrate and other aliphatic ketone hydrates are

the least stable ketone hydrates. Carbonic acid is somewhat of an anomaly: it has a very unusual dihydroxymethylene structure and a low stability constant, $K_{ST}$.

**Table 2.** Stability constants ($K_{ST}$) for *gem*-diols.

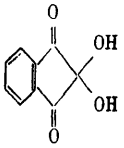
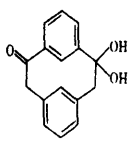
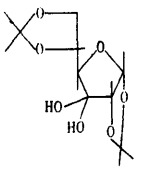
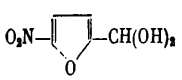
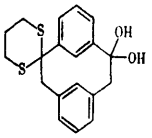
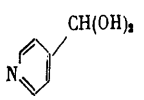
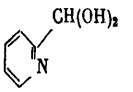
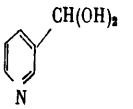
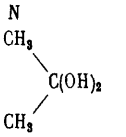
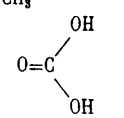
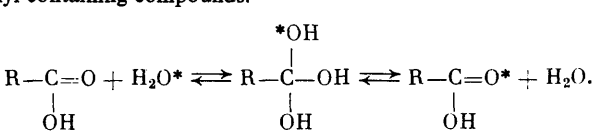
| Compound | Method of analysis | $K_{st}$ | Refs. |
|---|---|---|---|
| $CCl_3$—$CH(OH)_2$ | a | $2.78 \cdot 10^6$ | [5, 6] |
|  | a | $2.9 \cdot 10^5$ | [22] |
| $H_2C(OH)_2$ | a, b | $1.9 \cdot 10^5$ | [5, 6] |
| O=C—$CH(OH)_2$ \| OH | b | $1.8 \cdot 10^5$ | [21] |
| $CH_2Cl$—$CH(OH)_2$ | a | $3.7 \cdot 10^3$ | [5, 6] |
| O=C—$CH(OH)_2$ \| $O^-$ | b | $6.2 \cdot 10^3$ | [21] |
|  | c | 10 | [57] |
|  | a | 5.25 | [58] |
| O=C—C(OH)$_2$ \| \| HO $CH_3$ | a | 2.4 | [5, 6, 66] |
| O=C—C(OH)$_2$ \| \| $H_3C$ $CH_3$ | c | 2.1 | [67, 68] |
| $CH_3$—$CH(OH)_2$ | a, c | 1.43 | [5, 6] |
| O=C—C(OH)$_2$ \| \| HO $C_2H_5$ | a | 1.40 | [5, 6] |
|  | c | ~1.26 | [50] |
|  | c | 0.82 | [57] |
|  | a, b | 0.80–0.96 | [21] |

**Table 2** (continued).

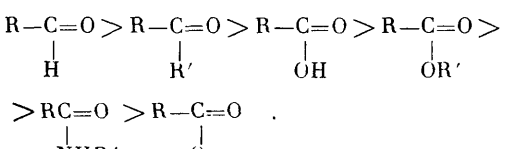
| Compound | Method of analysis | $K_{st}$ | Refs. |
|---|---|---|---|
|  | a, b | 0.20–0.67 | [21] |
|  | a | 0.11 | [21] |
|  | c | $2 \cdot 10^{-3}$ | [66] |
|  | d | $2.6 \cdot 10^{-4}$ | [5, 6] |

Note. a, UV- and IR-spectroscopy; b, polarography; c, NMR spectroscopy; d, electrical conductance.

There is no reference in the literature to the hydration of carboxyl groups to give 1,1,1-triols, sometimes referred to as orthocarboxylic acids. Derivatives of the latter, however, are well defined.[11] Indirectly, the formation and cleavage of 1,1,1-triols from carboxylic acids in water can be inferred by studying isotopic exchange of oxygen with the solvent; this has also been applied to other carbonyl-containing compounds.[69–73]



This mechanism is supported by the fact that no such oxygen exchange takes place with aliphatic alcohols or with phenols which display no tendency to undergo keto-enol tautomerism. With glucose only the carbonyl group is exchanged. The rate of oxygen exchange in acetone is very low compared with that of acetaldehyde. However, in the presence of aluminium oxide or silicon dioxide, the rate of oxygen exchange in acetone is enhanced due to the participation of the oxygen atoms of the catalyst.[74] Carboxylic acids exchange oxygen with the solvent more slowly than aldehydes. The rate of oxygen exchange of various carbonyl compounds decreases in the following sequence:[73]



For a given class of carbonyl compound, the rate depends to a large extent on the nature of the substituents. Thus, for substituted acetic

acids, the rate of exchange, as determined by IR-spectroscopy, is in the order:[75]

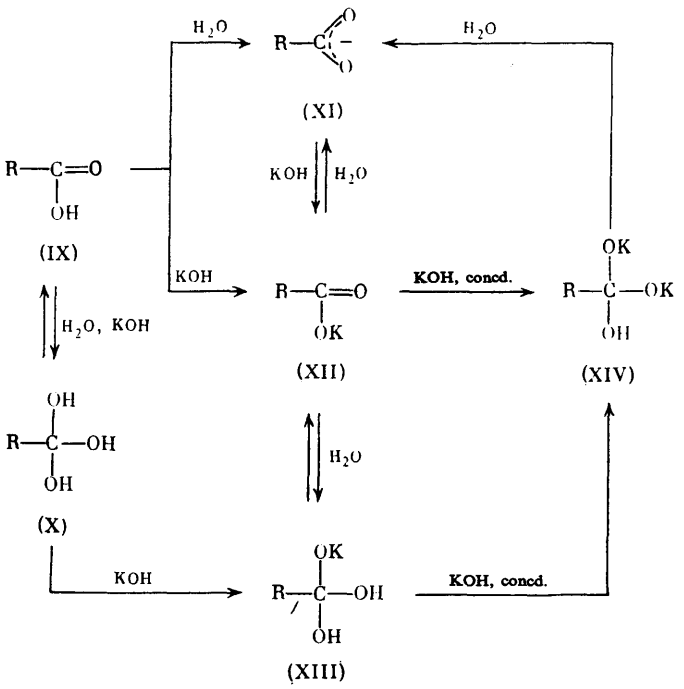
$$CF_3-COOH>CCl_3-COOH>CH_3-COOH>C(CH_3)_3-COOH$$

Benzaldehydes also readily undergo isotopic exchange by oxygen.[72] Electron-accepting substituents enhance the process while electron-donating groups have the opposite effect. Such evidence confirms that aromatic aldehyde hydrates have low stability: a fact that may not be apparent by other analytical techniques.

Thus, isotopic oxygen exchange, which has been studied with both carbonyl-containing compounds and inorganic oxide analogues.[70,71] can demonstrate the formation of all theoretically possible *gem*-polyol structures in solution. A dynamic equilibrium is set up, the position of which depends on many internal and external factors. In this context, it is interesting to study the reality of orthocarboxylic acids.

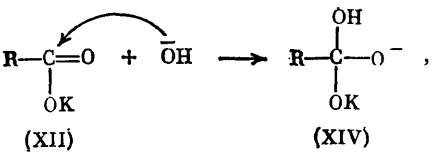
During the last few years a number of acid salts of orthocarboxylic acids (XIV) have been prepared by treatment of aqueous solutions of the corresponding carboxylic acid with concentrated base ($>5$ *N*). Such derivatives of benzoic furoic, sorbic, methacrylic acid, and others, have been prepared by this route.[9,76–78]

Scheme 2

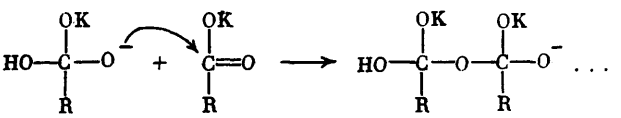



It is possible that what chemists have assumed to be simple potassium carboxylates (XII), formed in routine syntheses, are in fact orthocarboxylic acid salts (XIV). With either salt, routine hydrolysis with mineral acid would give the corresponding carboxylic acid (IX). Salts (XIV) are colourless compounds which are not readily soluble in $>5$ *N* base. In water, such orthocarboxylic acid salts are converted into the carboxyl forms (XI) and (XII).

Scheme 2 illustrates the various pathways leading to the formation of orthocarboxylic acids and their salts. While the dissociated acid and its salts are converted in water to the carboxyl anion (XI), which is normally unaffected by base, treatment with highly concentrated base provides suitable conditions for the formation of the undissociated salt (XII) as well as the corresponding orthocarboxylic acids (X) and orthocarboxylic acid salts (XIII) as a result of catalytic hydration. The formation of orthocarboxylic acid salts (XIV) may proceed either by nucleophilic addition of hydroxide ion to the carbonyl carbon of the carboxylate salt form (XII),




or by acid-base interaction of the monopotassium salt (XIII) with base in a second deprotonation. It is not possible to form the corresponding tripotassium orthocarboxylates under these conditions, presumably because of the weak acidity of the third hydroxy group. The structures of salts (XIV) have been confirmed by elemental analysis, IR spectroscopy (the absorption corresponding to $\nu_{C=O}$ being absent and that corresponding to $\nu_{OH}$ being present), and by potentiometric titration of the mixture of carboxylic acid salts and base obtained after cleavage of (XIV) in water. By the latter technique, it has been possible to determine the molecular weight and the proportion of inorganic anion and base in adduct (XIV). Thus, for salts of unsaturated carboxylic acids (cinnamic, acrylic, sorbic acids) it has been found that the adduct has a more complex structure in which one molecule of base is shared by 2–3 molecules of anion as a result of polymerisation.



Thus, although orthocarboxylic acids have not been demonstrated as stable species, their existence and properties have been inferred through the acid-base conversions of carboxylic acid salts in basic media.

Bases, as either reagents or catalysts, markedly accelerate hydration of carbonyl compounds relative to hydration in neutral media. A relationship has been established between the equilibrium constant for hydration ($K_{H_2O}$), the constant $K_{OH}$, for the adduct formation from aromatic aldehydes and hydroxide ion, and the acid dissociation constant, $K_a$, for the corresponding *gem*-diols ($K_w$ being the dissociation constant for water).[79]

The final product of the reaction is the acid salt of the corresponding metacarboxylic acid (XVI), the formation of which may arise by interaction of base with the metacarboxylic acid itself

or its anhydride, i.e. the aldehyde form. Much work, principally undertaken by Zuman et al., has been devoted to a study of this equilibrium and its mechanism.[80–85]

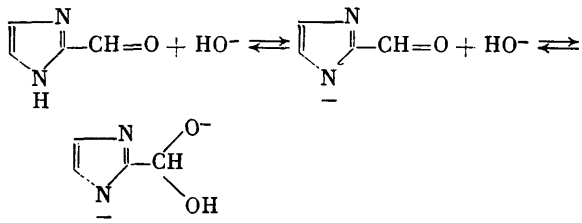
$$ArCH{=}O + HO^- \overset{K_{OH}}{\rightleftharpoons} ArCH(OH)O^-$$
(XVI)

$$H^+ \updownarrow K_w \qquad K_a \updownarrow H^+$$

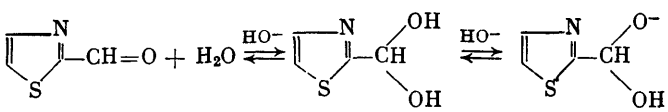
$$ArCH{=}O + H_2O \overset{K_{H_2O}}{\rightleftharpoons} ArCH(OH)_2$$
(XV)

$$K_a = K_{OH}\frac{K_w}{K_{H_2O}}$$

The reactions of a number of aromatic and heteroaromatic aldehydes with base have been reported.[80,81] Benzaldehyde and its derivatives, as well as furan-, thiophene- and *N*-methylpyrrole-carboxaldehydes, add hydroxide ion directly in one step to give the corresponding salt (XVI). Pyrrole- and pyrazole-carboxaldehydes react with base in two steps, the initial step being *N*-deprotonation.

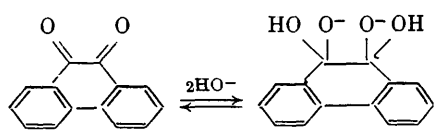


Thiazole-2-carboxaldehyde is initially hydrated, and then reacts with base as follows:



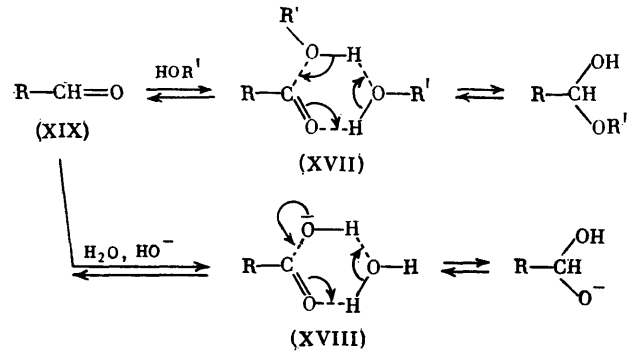
Evidently pyridinecarboxaldehydes also interact with base according to this scheme since a polarographic study in media containing a high concentration of base has established that three forms exist: a carbonyl, a *gem*-diol and an anionic form (XVI).[83]

While hydration of α-polyketones usually involves only one carbonyl group, addition of water or hydroxide ion to a second keto group may take place in the presence of base. This is evident with ninhydrin[22] (see above). It has also been shown that 9,10-phenanthrenequinone forms a stable dianion:[84]



The p$K_a$ values for a number of structurally varied *gem*-diols, given in Table 3, confirm the weakly acidic nature of these compounds. From these values for benzaldehyde derivatives, the corresponding values, $J_-$, $J_{m-}$ and $H_-$, $H_{m-}$, have been calculated.[81,82,85] These denote, respectively, the readiness of the OH and OR group to add to the carbonyl group, (C=O), and the interaction of these with protic solvents.

All of the examples studied are characterised by a final step involving the formation of the corresponding *gem*-polyol and its salt form. However, as has already been noted in review articles,[61,62] the formation of complex cyclic solvates or transition states precedes this stage. By studying the UV spectra of aromatic and heteroaromatic aldehydes in polar and non-polar solvents, an attempt has been made to analyse the spectra of solvate complexes, (XVII) and (XVIII), and calculate their stability constants.[89,90]



As solvation is reversible in polar media, aldehydes may exist in at least two forms—an unassociated carbonyl form (XIX) and a solvated form (XVII or XVIII)—as is the case with many other compounds which are solvated. This mixture of the two forms has been studied by measuring their light absorption properties. In particular, it has been established that benzaldehyde, as a dilute solution in water, is solvated to the extent of 70%, while the figure in ethanol is 54%. The corresponding values for *p*-nitrobenzaldehyde are 61 and 45%. Solvate complexes have well-defined UV-spectra so that the proportion of free and solvated forms in the mixture can be determined quantitatively. It cannot for certain be inferred that solvate complexes are necessarily converted into *gem*-diols or their derivatives, but their formation does represent an integral stage in the overall process.

**b) Characteristic reactions of *gem*-polyols**

Differences in the reactivity of hydrated and non-hydrated carbonyl complexes have, up to now, not been considered. It has been thought that these reactions are one and the same, except in certain instances. It is now clear, from the evidence presented, that carbonyl compounds and *gem*-diols are distinct functional groups, and that the latter, just as acetals, may in part fulfil the role of a masking group for the former. However, apart from their masking, accelerating and inhibiting properties towards the carbonyl function, *gem*-polyols do undergo reactions which are uniquely their own.

It has been argued that the degree of hydration of the carbonyl group may be an indication of its reactivity.[91] Thus, glutathione (GSH) only forms hemimercaptals with readily hydrated aldehydes and ketones. Glyoxal, which exists as a dihydrate in aqueous solution, affords two types of hemimercaptal, while methylglyoxal monohydrate forms only a ketohemimercaptal:

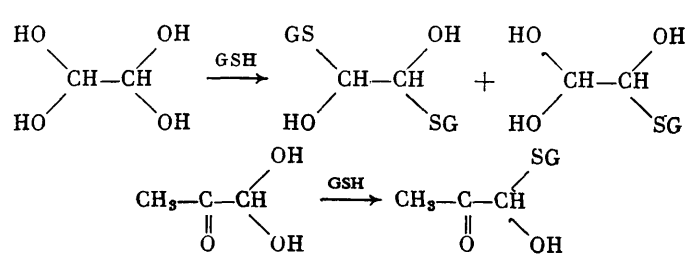
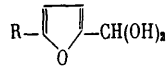
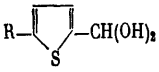
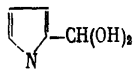
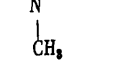
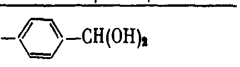
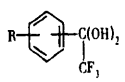
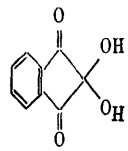


**Table 3. Values of the first dissociation constant ($pK_a$) for *gem*-diols.**

| Compound | $pK_a$ | Refs. |
|---|---|---|
| R-CH(OH)$_2$ | | |
| R=H | 12.70 | [5, 6, 86] |
| $CH_3$ | 13.57 | [5, 6, 86] |
| $(CH_3)_2CH$ | 13.77 | [5, 6, 86] |
| $CCl_3$ | 10.44 | [5, 6, 86] |
| $CH_3C(=O)$ | 11.00 | [86] |
|  | 12.05 | [86] |
|  | 13.00 | [86] |
|  | | |
| R=H | 14.75 | [80, 87] |
| $CH_3$ | 15.65 | [80, 87] |
| $NO_2$ | 11.82 | [80, 87] |
|  | | |
| R=H | 15.21 | [80, 87] |
| Br | 14.64 | [80, 87] |
|  | | |
|  | 17.50 | [80] |
|  | | |
| R=H | 14.90 | [86] |
| $CH_3$ | 15.39 | [86] |
| $OCH_3$ | 15.96 | [86] |
| $NO_2$ | 12.79 | [86] |
|  | | |
| R=H | 10.00 | [86] |
| *p*-$CH_3$ | 10.15 | [86] |
| *p*-$OCH_3$ | 10.18 | [86] |
| *m*-Br | 9.51 | [86] |
| *m*-$NO_2$ | 9.18 | [86] |
|  | 8.6 | [8] |
| $O{=}C(OH)_2$ | 3.7 | [88] |

It has also been established that the formation of pyrazines by condensation of *o*-phenylenediamine with trifluoromethylglyoxal proceeds with participation of a hydrated carbonyl group.[92] X-Ray structural analysis and NMR spectroscopy indicates that, of the three possible hydrated forms of the ketoaldehyde, the ketone hydrate (XX) is directly involved.

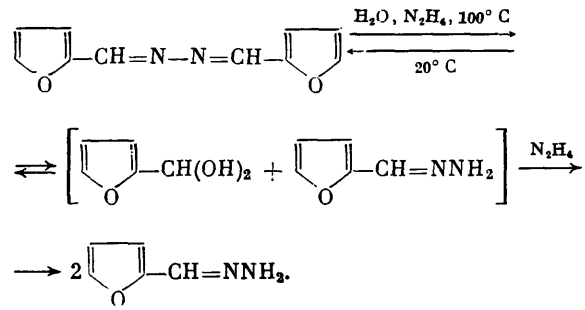
$$F_3C{-}C(=O){-}CH(=O) \overset{H_2O}{\rightleftharpoons} F_3C{-}C(OH)_2{-}CH(=O) \overset{H_2O}{\rightleftharpoons} F_3C{-}C(OH)_2{-}CH(OH)_2$$

(XX)

Initially, condensation takes place with the free aldehyde group; the hydrated keto group is then slowly dehydrated over 18 h at 23 °C prior to ring closure.

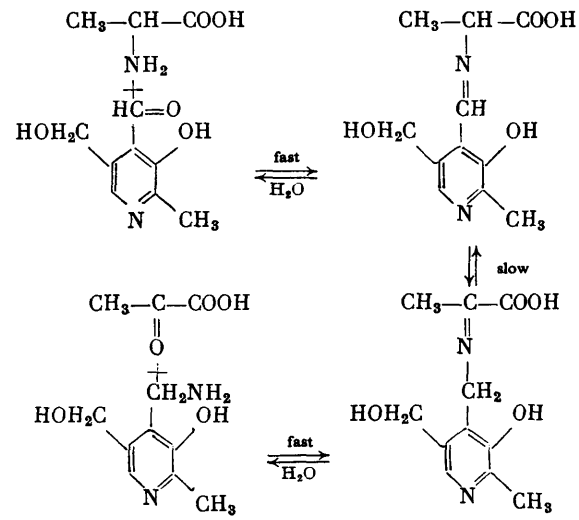
While in the above reaction it is apparent that the hydrated form hinders condensation, in other instances quite the reverse occurs, i.e. hydration facilitates condensation with amino groups. This is well illustrated in the review articles devoted to the chemistry of ninhydrin and analogues.[7,8] 4-Pyridinecarboxaldehyde hydrate has been recommended as a highly sensitive analytical reagent for phenylhydrazine and other unsymmetrically substituted hydrazines.[46] Interestingly, the analysis is not complicated by the presence of such reactive compounds as ammonia, hydroxylamines, aliphatic amines and aldehydes, acetone, etc.

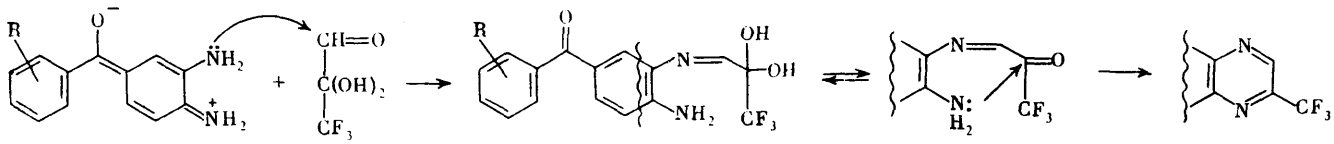
Evidently, the fact that aldehydes are not readily hydrated is reflected in the hydrolytic cleavage of the azomethine group. Thus, furfural hydrazone is obtained by heating the corresponding azine in aqueous hydrazine:[93]



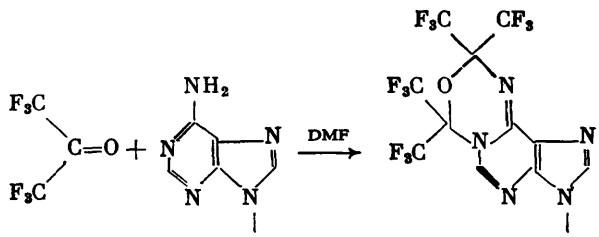
At 20 °C the equilibrium is shifted towards the azine.

Such conversions have a direct bearing on biological processes, as has been demonstrated.[94,95] Thus, in model studies of transferase-catalysed transamination,[94] the authors have discovered a reversible isomerisation of Schiff bases which, on hydrolysis, are converted [in the example below] to pyruvic acid or a substituted pyridine-4-carboxaldehyde. Both products are readily hydrated carbonyl compounds (a fact which the authors did not heed).

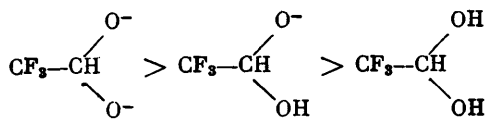




Hexafluoroacetone, which is also readily hydrated,[31,42–44] interacts with adenine and its derivatives to give a product derived by condensation with both the amino group and an endocyclic nitrogen atom.[95]

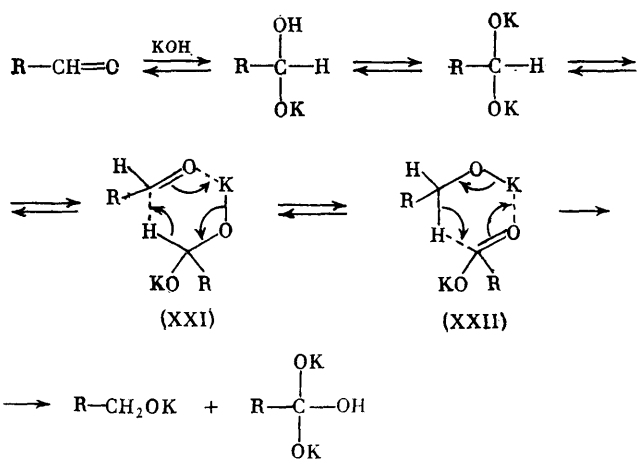


In heterogeneous redox reactions, carbonyl compounds and *gem*-diols perform opposing roles: the former as an oxidant and the latter as a reductant (i. e. as a typical alcohol). In the case of fluoral hydrate, it has been shown that the reducing power increases as the concentration of base increases since the anionic form of the diol is a better oxidant than the neutral molecule:[88]



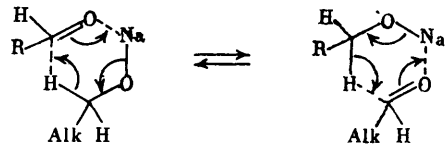
Oxidation of *gem*-polyols is accompanied either by loss of hydride ion[18,96] or, under more forcing conditions, by heterolytic cleavage of a carbon–carbon bond.[19]

For the disproportionation of furancarboxaldehydes on the surface of base granules under an inert atmosphere (in toluene, benzene or diethyl ether [not absolute]), it has been suggested that reaction proceeds via a cyclic complex (XXI) formed from one molecule of aldehyde and one of the corresponding *gem*-dialkoxide. This is converted to (XXII) by hydride transfer, in much the same way as a tautomeric rearrangement. It is an established fact that aromatic alcohols are formed from various aromatic aldehydes in the presence of formaldehydes.[2,18,96] The latter, functioning as a stable *gem*-diol, serves as a reductant, being oxidised by the same type of bond reorganisation depicted in complex (XXI).



(XXI) (XXII)

Simple aliphatic alcohols may perform the same function. Thus, a similar redox interaction has been proposed for the reaction of furfural with simple alkoxides:[97]



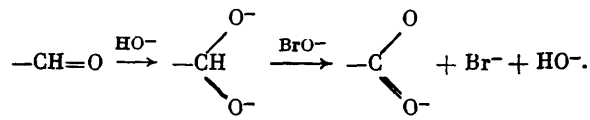
The familiar Meerwein–Pondorff–Verley–Oppenauer conversion with aluminium alkoxides[99] can thus be effectively performed with sodium alkoxides. The resulting aliphatic aldehyde may take part in a subsequent aldol condensation in the presence of an excess of aromatic or heteroaromatic aldehyde.[100]

Evidently, many established routes to carboxylic acids by oxidation of aromatic or heterocyclic aldehydes in basic media (notably Ref. 101) proceed via oxidation of a *gem*-dialkoxide. This has been confirmed for the hypohalite-mediated oxidation of furfural and its 5-methyl derivative.[102,103] A previously reported oxidation of furfural with sodium hypobromite[104] proved unsuccessful with 5-methylfurfural. However, 5-methyl-2-furoic acid was obtained in up to 95% yield by significantly increasing the amount of base (> 1 molar equivalent).

$$Br_2+2NaOH\rightarrow NaOBr+NaBr+H_2O,$$

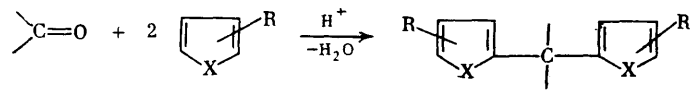
$$-CH=O+NaOBr+NaOH\rightarrow -COONa+NaBr+H_2O.$$

This would suggest that oxidation by hypobromite ion proceeds via the *gem*-dialkoxide rather than directly on the aldehyde:



Excess of base enhances hydration of the carbonyl group, especially in 5-methylfurfural, where the methyl group reduces the polarisation of the carbonyl function.

Under acidic catalysis, all forms of the carbonyl compound (hydrated or non-hydrated ketones and aldehydes) condense with aromatic systems to give polyaryl- or polyheteroaryl-alkanes:[105–107]

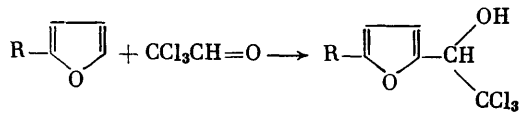


(XXIII)

X = CH = CH, O, S etc. R = H, Alk, OH, OAlk, Hal etc.

Reaction proceeds in two stages with the intermediate formation of secondary or tertiary alcohols (as is the case with alkylation). Termination of the reaction at this intermediate stage is relatively easy for carbonyl compounds which are readily hydrated, while reaction goes to completion in all other cases. In the case of chloral, condensation with various arenes affords the insecticide DDT and its analogues (XXIII, where X = CH = CH),[107] i. e. reaction goes to completion; however, the reaction of anhydrous chloral with furan

derivatives in the presence of $AlCl_3$ yields the corresponding secondary alcohol in up to 75% yield:[108]

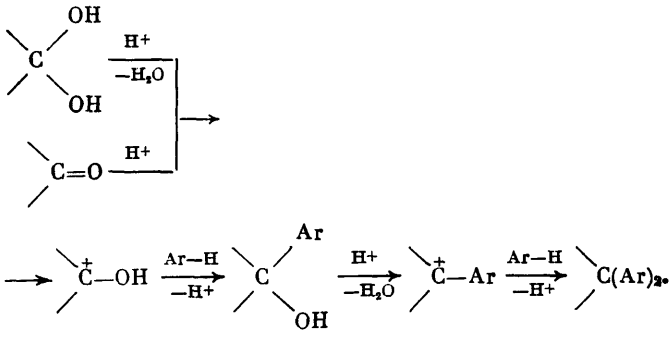


R = H, $CH_3$, COOAlk.

The same product is obtained from chloral hydrate in sulphuric acid.

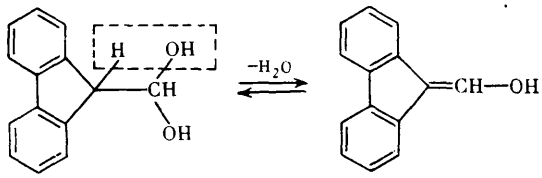
Trifluoropyruvic acid[109] and hexafluoroacetone,[110] which are even more readily hydrated, react in the same way with furan, thiophene, and *N*-methylpyrrole, even in the absence of catalyst.

It is known that electron-accepting (polyhalogeno) groups not only stabilise *gem*-diols but also inhibit the subsequent condensation of the intermediate secondary or tertiary alcohols with a second arene molecule. In the absence of such groups, the process continues (stage B), in the same way as aromatic alkylation with alcohols.



(A) (Б)

The formation of enols from *gem*-diols is interesting. Thus, 9-formylfluorene hydrate, having a labile α-hydrogen at $C_9$, dehydrates to give the corresponding enol.[111,112] In aqueous solution the *gem*-diol : enol ratio is 1 : 3.



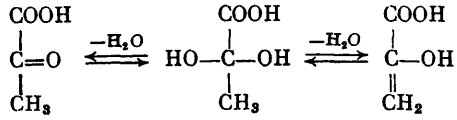
The enol group may be hydrated to reverse the reaction. Hydroxide ion accelerates the process. By comparison with simple alkenes, hydration of enols is four times faster.

$$(CH_3)_2C{=}CH{-}OH + H_2O \overset{K_1}{\rightleftarrows} (CH_3)_2CH{-}CH(OH)_2,$$

$$(CH_3)_2C{=}CH_2 + H_2O \overset{K_2}{\rightleftarrows} (CH_3)_2CH{-}CH_2{-}OH,$$

$$\lg(K_1/K_2) = 3.9.$$

Aqueous solutions of pyruvic acid contain three forms: a carbonyl, an enol and a *gem*-diol.[87] The *gem*-diol is considered to be an intermediate structure.

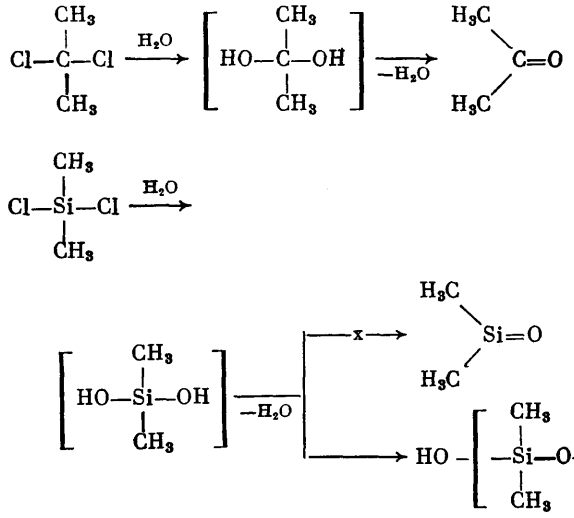


That *gem*-diols may be implicated in enolisation has been noted, especially by Toullec.[113]

## III. *gem*-Polyols as members of the *gem*-polyhydroxide family

The reversible hydration of carbonyl groups is in many respects identical with the interconversion of oxides and hydroxides, and effectively is a special case of the latter. The stability and reactivity of *gem*-polyols can be examined in a whole series of related structures by taking into account the characteristics of each system as determined by the central atom. Such comparative studies, however, have rarely been reported. In recent years, quantum mechanics has shed light on the configuration, energy, bond lengths and other parameters pertaining to polyhydroxides of general structure $T(OH)_n$, where T = C, Si, B, Al, Sn and others; $n = 2-4$.[114,-117]

Of group IV elements, only carbon is reluctant to form polyhydroxides. Thus, hydrolysis of 2,2-dichloropropane affords acetone, while dichlorodimethylsilane gives a polysiloxane.[118]



In aqueous ammonia, stannic chloride is hydrolysed to $Sn(OH)_4$ — stannic acid.[119] However, hydrolysis of carbon tetrachloride, like the hydration of carbon dioxide,[63,120] affords dihydroxycarbon monoxide, i.e. carbonic acid

$$O{=}C{=}O + H_2O \rightleftharpoons O{=}C(OH)_2.$$

At the same time, the possibility of forming tetrahydroxycarbon (tetraol) in solution has been indicated by studies of isotopic oxygen exchange.[70,71] These have revealed that the rate of oxygen exchange increases with the atomic number of the central atom, which coincides with an increase in the stability of the polyhydroxide.

The fact that carbon dioxide is only partially hydrated, and anomalies in the hydration of carbonyl compounds, can be viewed with the properties of a large number of polyoxides, which also interact with water to give a variety of hydrated compounds, notably polybasic inorganic acids. The possible factors responsible for the formation of such compounds have been examined earlier.[120,121] The stability of polyhydroxides increases with the atomic number of the central atom and with the Periodic Group number. This is determined by the strength of the T—O bond. Thus, for the halogens in the maximum oxidation state, chlorine forms a monohydroxide, i.e. perchloric acid [$HOCl(=O)_3$], whereas iodine forms $(HO)_3I(=O)_2$. For sulphur, the dihydroxide is known ($H_2SO_4$), but for tellurium the analogue is $Te(OH)_6$. For nitrogen,

the monohydroxide ($HNO_3$) is known, but phosphorus forms both meta- and ortho-acids [$HOP(=O)_2$, $(HO)_3P=O$, and others] as the corresponding anhydride, $P_2O_6$, can be hydrated to various degrees. The stability of these polyhydroxides is determined by many factors inherent in the structure of the central atom. In this respect, a key role is played by vacant orbitals,[122] which give rise to partial double character as a result of a shift of a lone pair of electrons from oxygen:



For carbon compounds which lack vacant orbitals, such stabilisation can be achieved by neighbouring electron-accepting groups which lower the electron density at the carbon atom. Other factors, such as the anomeric effect[123] also have a stabilising effect. The fact that many *gem*-diols are stable only in solution, and are formed as reaction intermediates, would also argue in favour of another stabilising factor: the formation of complex solvates. The full analysis of this aspect would require a separate review.

## References


1. A M Butlerov *Sochineniya* (Essays), Izd. AN SSSR, Moscow, 1953, Vol. 2, pp. 157, 270
2. S K Ogorodnikov *Formal'degid* (Formaldehyde), Khimiya, Leningrad, 1984, p. 84
3. *Universal'naya Desyatichnaya Klassifikatsiya. Estestvennye Nauki* (Universal Decimal Classification. Natural Sciences), Izd. Standartov, Moscow, 1983, Vol. 2, No. 1, p. 199
4. A P Nechaev *Organicheskaya Khimiya* (Organic Chemistry), Izd. Vyssh. Shk., Moscow, 1988, p. 120
5. R P Bell *Adv. Phys. Org. Chem.*, 1966, **4** 1
6. R Bell *Novye Problemy Fizicheskoi Organicheskoi Khimii* (New Problems of Physical Organic Chemistry), Mir, Moscow, 1969, p. 236
7. D J McCaldin *Chem. Rev.*, 1960, **60** 39
8. V P Oshkaya *Ningidrinovye Reaktsii* (Reactions of Ninhydrin), Zinatne, Riga, 1974, p. 174
9. Yu M Shapiro *Khimiya i Tekhnologiya Furanovykh Soedinenii* (Chemistry and Technology of Furan Compounds), Izd. KPI, Krasnodar, 1988, p. 48
10. L A Yanovskaya, S S Yufit, V F Kucherov *Khimiya Atsetalei* (Chemistry of Acetals), Nauka, Moscow, 1975, p. 275
11. R H De Wolfe *Carboxylic Ortho Acid Derivatives*, Acad. Press., New York–London, 1970, 557 pp
12. V V Mezheritskii, E P Olekhnovich, S M Luk'yanov, G N Dorofeenko *Orto-efiry v Organicheskom Sinteze* (Orthoesters in Organic Synthesis), Izd. Rostov University, Rostov-on-Don, 1976, p. 176
13. S G Warren *Chemistry of the Carbonyl Group*, Wiley and Sons, New York–London, 1974
14. F Kerri, R Sandberg *Uglublennyi Kurs Organicheskoi Khimii* (Complex Transformations in Organic Chemistry), Khimiya, Moscow, 1981, Book 1, p. 291
15. R Brettl *Obshchaya Organicheskaya Khimiya* (General Organic Chemistry) (Edited by D Barton, W D Ollis), Khimiya, Moscow, 1982, Vol. 2, p. 488
16. I O Sazerland *Obshchaya Organicheskaya Khimiya* (General Organic Chemistry) (Edited by D Barton, W D Ollis), Khimiya, Moscow, 1983, Vol. 4, p. 288
17. M Bender, R Bergeron, M Komiyama *Bioorganicheskaya Khimiya Fermentativnogo Kataliza* (Bioorganic Chemistry of Enzymatic Catalysis), Mir, Moscow, 1987, pp 56, 154
18. Z N Parnes, D N Kursanov *Reaktsii Gidridnogo Peremeshcheniya v Organicheskoi Khimii* (Hydride Transfer Reactions in Organic Chemistry), Nauka, Moscow, 1969
19. G A Artamkina, I P Beletskaya *Usp. Khim.*, 1987, **56**(10) 1717 [English translation in *Russ. Chem. Rev.*, 1987(10)]
20. A N Nesmeyanov, N A Nesmeyanov *Nachala Organicheskoi Khimii* (The Beginnings of Organic Chemistry), Khimiya, Moscow, 1974, Vol. 1, pp 294, 313
21. Ya I Tur'yan *Khimicheskie Reaktsii v Polyarografii* (Chemical Reactions in Polarography), Khimiya, Moscow, 1980, p. 267
22. W Knocke, H Wendt, M-L Ahrens, H Strehlow *Collect. Czech. Chem. Commun.*, 1966, **31** 388
23. R Gleiter, W Dobler *Chem. Ber.*, 1985, **118** 4725
24. A Schönberg, E Singer *Chem. Ber.*, 1971, **104** 160
25. A Schönberg, M Mamluk *Chem. Ber.*, 1972, **105** 1562
26. C Sandris, G Ourisson *Bull. Soc. Chim. Fr.*, 1958, 338
27. C Sandris, G Ourisson *Bull. Soc. Chim. Fr.*, 1956, 958
28. H Patting, H Strehlov *Ber. Bunsenges. Phys. Chem.*, 1969, **73** 534
29. Y Pocker, J E Meany *J. Phys. Chem.*, 1970, **74** 1486
30. H-J Buschman, W Knocke *Ber. Bunsenges. Phys. Chem.*, 1977, **81** 72
31. I L Knunyants et al. *Dokl. Akad. Nauk SSSR*, 1966, **169** 954
32. V I Saloutin, I A Piterskikh, K I Pashkevich, et al. *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1980, (10) 2403
33. A M Fomin, V I Saloutin, K I Pashkevich, et al. *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1983, (11) 2626
34. V I Saloutin, I A Piterskikh, K I Pashkevich, et al. *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1986, (3) 625
35. P Federlin *Bull. Soc. Chim. Fr.*, 1953, 11
36. V M Korobkov, I V Nyukhina, V G Barinov, USSR P. 435 226; *Byull. Izobret.*, 1974, (25) 78
37. B A Geller, L F Kulish, I G Khaskin, G K Rudnev *Teor. Eksp. Khim.*, 1975, **11** 100
38. B A Geller, I G Khaskin, L K Skrunts *Zh. Obshch. Khim.*, 1985, **55** 355
39. P E Sörensen *Acta Chem. Scand., Ser. A*, 1976, **30**(9) 673
40. E M Schulman, O D Bonner, D R Schulman, F M Laskovics *J. Am. Chem. Soc.*, 1976, **98** 3793
41. K Veigand, G Khil'getag *Metody Eksperimenta v Organicheskoi Khimii* (Experimental Techniques in Organic Chemistry), Khimiya, Moscow, 1968, p. 175
42. A Khen, R Pelli, R Al'm *Khimiya Ftora* (Chemistry of Fluorine) (Edited by I L Knunyants et al.), Izd. Inostr. Lit., Moscow, 1952, Ch. 3, p. 209
43. N Fukuhara, L A Bigelow *Khimiya Ftora* (Chemistry of Fluorine) (Edited by I L Knunyants et al.), Izd. Inostr. Lit., Moscow, 1952, Ch. 3, p. 220
44. A Khen, D Shepard, M Yung *Khimiya Ftora* (Chemistry of Fluorine) (Edited by I L Knunyants et al.), Izd. Inostr. Lit., Moscow, 1952, Ch. 3, p. 229
45. R R Soelsh, E McNierney, C A Tannenbaum, et al. *J. Org. Chem.*, 1989, **54**(23) 5502
46. L Ya Leitis et al. *Izv. Akad. Nauk LatvSSR*, 1983, (8) 96

47. J March *Organicheskaya Khimiya* (Advanced Organic Chemistry, 3rd Edition, Wiley Interscience, p. 325), Mir, Moscow, 1987, Vol. 3, p. 325
48. Y Pocker, J E Meany *J. Phys. Chem.*, 1969, **73** 1857
49. E Laviron, J Tirouflet *Compt. Acad. Sci.*, 1959, **248** 826
50. R W Busker, G M J Beijersbergen van Henegouwen, K Erkelens *Heterocycles*, 1987, **26**(1) 5
51. M V Rubtsov, A G Baichikov *Sinteticheskie Khimiko-farmatsevticheskie Preparaty* (Synthetic Chemical Pharmaceutical Preparations), Meditsina, Moscow, 1971, p. 179
52. S D Fedoryak et al. *Khim.-farm. Zh.*, 1982, **16**(1) 48
53. H C Brown, R S Fletcher, R B Johannesen *J. Am. Chem. Soc.*, 1951, **73** 212
54. S E Schaafsma, H Steinberg, Th J de Boer *Recl. Trav. Chim. Pays-Bas*, 1967, **86**(6) 651
55. N J Turro *Acc. Chem. Res.*, 1969, **2** 25
56. H H Wasserman, C M Clark, P C Turley *Top. Curr. Chem.*, 1974, **47** 73
57. D Krois, E Langer, H Lehner *Tetrahedron*, 1980, **36** 1345
58. K N Slessor, A S Tracey *Can. J. Chem.*, 1969, **47**(21) 3989
59. K N Slessor, A S Tracey *Can. J. Chem.*, 1976, **48**(18) 2900
60. K N Slessor, A S Tracey *Carbonyl. Res.*, 1973, **27** 407
61. V I Minkin, B Ya Simkin, R M Minyaev *Kvantovaya Khimiya Organicheskikh Soedinenii. Mekhanizmy Reaktsii* (Quantum Chemistry of Organic Compounds. Reaction Mechanisms), Khimiya, Moscow, 1986, p. 125
62. B Ya Simkin, I I Sheikhet *Kvantovokhimicheskaya i Statisticheskaya Teoriya Rastvorov* (Quantum Chemical and Statistical Theory of Solutions), Khimiya, Moscow, 1989, p. 228
63. D M Kern *J. Chem. Educ.*, 1960, (1) 14
64. A E Agronomov *Izbrannye Glavy Organicheskoi Khimii* (Selected Aspects of Organic Chemistry), Moscow State University, Moscow, 1975, p. 95
65. I I Stepuro et al. *Zh. Fiz. Khim.*, 1984, **58**(4) 929 [English translation in *Russ. J. Phys. Chem.*, 1984(4)]
66. P Greenzaid, Z Luz, D Samuel *J. Am. Chem. Soc.*, 1967, **89** 749, 756
67. H-J Buschmann, H-H Füldner, W Knoche *Ber. Bunsenges. Phys. Chem.*, 1980, **84** 41
68. H-J Buschmann, E Dutkewicz, W Knocke *Ber. Bunsenges. Phys. Chem.*, 1982, **86** 129
69. M Cohn, H C Urey *J. Am. Chem. Soc.*, 1938, **60** 679
70. A I Brodskii *Khimiya Izotopov* (Chemistry of Isotopes), Izd. AN SSSR, Moscow, 1957, p. 306
71. A I Brodskii, N A Vysotskaya *Zh. Fiz. Khim.*, 1958, **32** 1521
72. M M Aleksankin, I P Gragerov *Zh. Obshch. Khim.*, 1961, **31** 3167
73. G P Miklukhin *Izotopy v Organicheskoi Khimii* (Isotopes in Organic Chemistry), Izd. AN Ukrainian SSR, Kiev, 1961, p. 314
74. R M Smirnova et al. *Kinet. Katal.*, 1975, **16**(5) 1341
75. R L Redington *J. Phys. Chem.*, 1976, **80**(3) 229
76. Yu M Shapiro *Produkty Vzaimodeistviya Solei Organicheskikh Kislot so Shchelochami* (Products of the Interaction of Salts of Organic Acids with Bases), Krasnodar, 1984, p. 5. Deposited in ONIITEKhim, Cherkass, 25.06.84, No. 600khpD84; *Ref. Zh. Khim.*, 1984, 20Zh108
77. Yu M Shapiro *XXXI Intern. Congress on Pure and Appl. Chem. Abstracts*, Sofia, Bulgaria, 1987, Vol. 2, pp 6, 168
78. Yu M Shapiro *Zh. Obshch. Khim.*, 1988, **58**(4) 947
79. P Greenzaid *J. Org. Chem.*, 1973, **38** 3164
80. W J Bover, P Zuman *J. Electrochem. Soc.*, 1975, **122** 368
81. W J Scott, W J Bover, K Bratin, P Zuman *J. Org.Chem.*, 1976, **41** 1952
82. W J Bover, P Zuman *J. Am. Chem. Soc.*, 1973, **95** 2531
83. J F Rusling, P Zuman *J. Electroanal. Chem.*, 1983, **213** 277
84. P Zuman *Microchem.*, 1987, **36** 54
85. B Jandik, P Zuman, L Meites *J. Chem. Soc., Faraday Trans. 1*, 1983, **79** 2721
86. *Tablitsy Konstant. Skorosti i Ravnovesiya Geteroliticheskikh Organicheskikh Reaktsii* (Tables of Constants. Rates and Equilibria of Heterolytic Organic Reactions) (Edited by V A Pal'm), VINITI, Moscow, 1975, p. 1
87. J Kozlovski, C German, P Zuman *Anal. Proc.*, 1986, **23** 742
88. R Stewart, M M Mocek *Can. J. Chem.*, 1963, **41** 1160
89. Yu M Shapiro *Kislorodosoderzhashchie Geterotsikly. Tez. Dokl. Vsesoyuz. Soveshchaniya* (Oxygen-containing Heterocycles. Abstracts of Reports of the All-Union Conference, Krasnodar), Izd. KPI, Krasnodar, 1990, p. 59
90. Yu M Shapiro *Khimiya i Tekhnologiya Furanovykh Soedinenii* (Chemistry and Technology of Furan Compounds), Izd. KPI, Krasnodar, 1990, p. 61
91. L Z Arikovskii, L V Bystrykh *Zh. Obshch. Khim.*, 1986, **56** 1397
92. M Gushman, H Patel, A McKenzie *J. Org. Chem.*, 1988, **53** 5088
93. Yu M Shapiro, O P Kravtsova *Izv. Vuzov., Khim. Khim. Tekhnol.*, 1982, **25**(12) 1443
94. B E C Banks, M P Bell, A J Lawrence, et al. *Khimiya i Biologiya Piridoksalevogo Kataliza* (Chemistry and Biology of Pyridoxal Catalysis), Nauka, Moscow, 1968, p. 120
95. V D Sviridov, N D Chkanikov, A F Kolomiets, A V Fokin *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1985, (11) 2554
96. T A Geissman *Organicheskie Reaktsii* (Organic Reactions) (Vol. 2 Edited by R Adams, Wiley, New York, 1944), Izd. Inostr. Lit., Moscow, 1950, Vol. 2, p. 106
97. Yu M Shapiro, V P Smolyakov, V G Kul'nevich *Khim. Geterotsikl. Soedin.*, 1990, (6) 741
98. Yu M Shapiro, V G Kul'nevich, USSR P. 519412; *Byull. Izobret.*, 1976, (24) 69
99. K V Vatsuro, G L Mishchenko *Imennye Reaktsii v Organicheskoi Khimii. Spravochnik* (Named Reactions in Organic Chemistry. Reference Book), Khimiya, Moscow, 1976, pp 303, 372
100. Yu M Shapiro, V G Kul'nevich, L P Lavrinenko, USSR P. 883 036; *Byull. Izobret.*, 1981, (43) 101
101. A A Ponomarev *Sintezy i Reaktsii Furanovykh Veshchestv* (Synthesis and Reactions of Furan Compounds, Saratovsk), Izd. Sarat. Univ., Saratovsk, 1960, pp 158, 159
102. Yu M Shapiro, O A Pustovarova, E Baum, V G Kul'nevich *Khim. Geterotsikl. Soedin.*, 1982, (11) 1463
103. Yu M Shapiro, O A Pustovarova, V G Kul'nevich, et al., USSR P. 592 825; *Byull. Izobret.*, 1978, (6)
104. A P Salchinkin, L B Lapkova *Zh. Prikl. Khim.*, 1956, **28** 141
105. Yu M Shapiro, V G Kul'nevich *Khimiya i Tekhnologiya Furanovykh Soedinenii. Tr. Krasnodarskogo Politekh. In-ta* (Chemistry and Technology of Furan Compounds. Reports of the Polytechnic Institute, Krasnodar), 1975, Vol. 66, p. 75
106. Z N Verkhovskaya *Difenilpropan* (Diphenylpropane), Khimiya, Moscow, 1971, p. 196

107. R L Metcalf, J Kapoor, A Hirve, US P. 3 787 505; *Ref. Zh. Biol.*, 1975, 1K23OP
108. M Uber, R Bartroli, L Lami, M Diaz *Chemistry of Heterocyclic Compounds* (Edited by J Kovac), Elsevier, New York–Toronto, 1988, p. 562
109. A S Golubev, A F Kolomiets, A V Fokin *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, (10) 2369
110. G I Nikishin, V G Glukhovtsev, Yu V Il'in, A V Ignatenko *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1982, (2), 447
111. M P Harcourt, R A M O'Ferrall *J. Chem. Soc., Chem. Commun.*, 1987, (11) 822, 823
112. M P Harcourt, R A M O'Ferrall *Bull. Soc. Chim. Fr.*, 1988, (2) 407
113. J Toullec *Adv. Phys. Org. Chem.*, 1982, **18** 1
114. A C Hess, P F McMillan, M O'Keeffe *J. Phys. Chem.*, 1988, **92** 1785
115. G V Gibbs, Ph D'Arno, M B Boisen, Jr. *J. Phys. Chem.*, 1987, **91** 5347
116. A E Reed, D Schade, P von R Schleyer, et al. *J. Chem. Soc., Chem. Commun.*, 1988, 67
117. B M Pinto, H B Schelegel, S Wolfe *Can. J. Chem.*, 1987, **65** 1658
118. L B Clapp *The Chemistry of the OH-groups*, Englewood Chiffs, New York, 1967
119. N G Klyuchnikov *Neorganicheskii Sintez* (Inorganic Synthesis), Izd. Prosveshchenie, Moscow, 1988, pp 28, 146
120. Ya L Ugai *Neorganicheskaya Khimiya* (Inorganic Chemistry), Izd. Vyssh. Shk., Moscow, 1989, pp 83, 188
121. C A Nenitzescu *Obshchaya Khimiya* (General Chemistry) (Chimie Generala, 2nd Edition, Bucharest, Editura Technica, 1963), Mir, Moscow, 1968, p. 340
122. V F Tikavyi *Zh. Neorg. Khim.*, 1977, **22**(1) 233 [English translation in *Russ. J. Inorg. Chem.*, 1977(1)]
123. A J Kirby *Anomernyi Effekt Kislorodsoderzhashchik Soedinenii* (The Anomeric Effect and Related Stereoelectronic Effects at Oxygen, Springer Verlag, New York, 1983), Mir, Moscow, 1985, p. 171