CHEMICAL PROPERTIES OF 3,6- AND 5,6-DIHYDRO-2H-PYRANS (REVIEW)

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The reactions of 3,6- and 5,6-dihydro-2H-pyrans that are due to the presence of double and ether bonds are correlated.

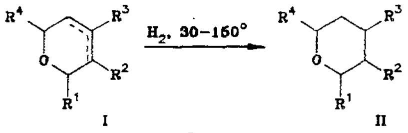
Owing to the advances in organic and petrochemical synthesis in the last 10 years, cyclic ethers such as 3,6- and 5,6-dihydro-2H-pyrans (DHP) have also become accessible [1-5]. This has stimulated intensive research on the chemistry of di- and tetrahydropyrans and has led to the development of new syntheses of natural compounds (citric acid, cis-3-hexen-1-ol, rose-oxide, etc.) and their analogs, which have valuable properties. Dihydropyrans can serve as convenient intermediates for organic synthesis. However, with the exception of a previous review [6], there have been no publications that correlate the properties of these compounds.

The present review encompasses virtually all of the known reactions of DHP (data on 2-alkoxy, hydroxy, and carboxy derivatives and pyrones are not included), which can be conveniently classified in the following way: addition to the double bond and isomerization, oxidative transformations, and reactions that are accompanied by ring opening.

ADDITION AND ISOMERIZATION REACTIONS

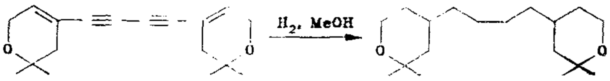
The hydrogenation of DHP is accomplished in both the liquid and gas phase with the use of ordinary (Pt, Pd, Ni) catalysts.

Alkyl-substituted DHP I are hydrogenated quite smoothly to II (76-95%) on Raney nickel in ether [7, 8], in ethanol [9, 10], or without a solvent [1].



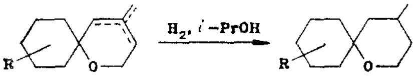
R^1, R^2, R^3, R^4 – H or Alk

Polyunsaturated diether III is hydrogenated virtually completely (95%) when Ni modified with 5% Mo is used [11].



III

Similar results were obtained in the hydrogenation of 2,2-dimethyl-4-vinylethynyl-3,6-dihydropyran on Pt_2O [12]. 4-Methyltetrahydropyran (IV) is formed in quantitative yield from an industrial pyran fraction at 120-180°C and atmospheric pressure on Ni/Cr_2O_3 [13] and on Pd/C (0.5% Pd) at 150-250°C [14]. An increase in the Pd content to 5% and an increase in pressure make it possible to carry out the reaction at room temperature (86% yield) [15]. Steric factors have an appreciable effect in the hydrogenation of spiro derivatives V on the same catalyst – the yield of products VI decreases substantially if R ≠ H or R ≠ Me [16].



V VI

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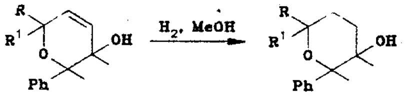
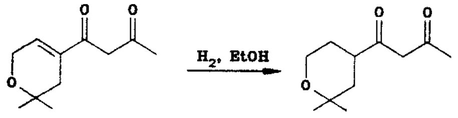
Functional derivatives of DHP behave like other substituted olefins under hydrogenation conditions. A number of examples illustrate the possibility of the selective addition of H_2 to the double bond of DHP. Palladium on carbon (Pd/C) was used in the synthesis of 2-acetonyl-4-methyltetrahydropyran [17, 18], while Pd/$CaCO_3$ was used in the synthesis of 2-trifluoromethyl-4-methyltetrahydropyran (98%) [19] and a number of hydroxytetrahydropyrans VIII [20] from the corresponding DHP VII.



VII VIII

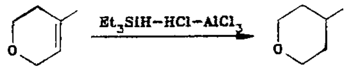
Similar results were also obtained in the hydrogenation of Pt_2O of 4,5-dimethyl-2-trichloromethyl-3,6-dihydropyran (96%) [21] and butanedione IX (75%) [22].



IX

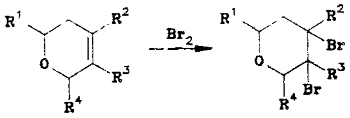
The DHP ring can be cleaved at the C–O bond when Pt metal is used. For example, amyl alcohol (38%) is formed along with tetrahydropyran (34%) from 5,6-dihydropyran (X) [23], while a mixture of hydrocarbons is formed from 4-methyl-5,6-dihydropyran (XI) [13].

Ionic hydrogenation is an alternative catalytic reaction of olefins with H_2. However, in the case of ether XI the yield of IV did not exceed 30-40%; this is due to a decrease in the relative reactivity of the double bond due to complexing of $AlCl_3$ with the heteroatom [24].



XI IV

The halogenation, particularly the bromination, of DHP has been described [21, 25-27]. Substituted olefins XII react smoothly with Br_2 (90-97%) at 0 to −70°C in ordinary halogen-containing solvents.

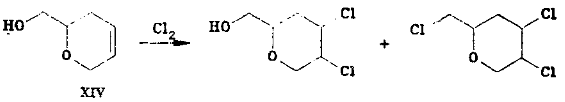


XII XIII

R^1, R^2, R^3, R^4=H, Alk, di- and trihaloalkyl, alkenyl

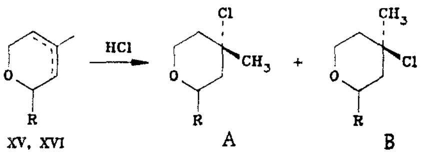
Such conditions are favorable for the formation of trans-dibromides, which should exist in the form of spatial isomers. However, the stereochemical aspects of the reaction are not discussed in the indicated studies.

Chlorine is more active in reactions with DHP; it is therefore not surprising that the trichloride is obtained along with the dichloride from XIV [28].



XIV

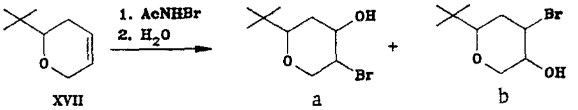
Examples of the reaction of DHP also with other halogen-containing reagents have been described in the literature. Thus the hydrochlorination of 4-methyl-2-isopropyl- and 4-methyl-2-isobutyl-dihydropyran (XV and XVI) [2, 29] proceeds in accordance with the Markownikoff rule and leads to a mixture (80%) of spatial isomers A and B with preponderance of the former.



XV R= *i*-Pr; XVI R= *i*-Bu

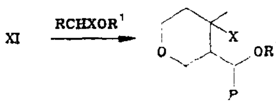
In both cases R occupies primarily an equatorial position; this explains the absence of the other two possible isomers.

The reaction of N-bromoacetamide with XVII in aqueous dioxane proceeds regioselectively with a:b = 9:1 [30, 31].



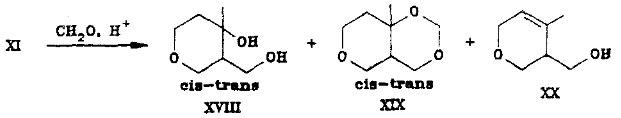
Compound X reacts similarly with tert-butyl hypochlorite [32]. The 3-bromo-4-hydroxy derivative is formed exclusively from 2,6-dimethyl-3-carboxy-5,6-dihydropyran and KBrO; this is explained by the presence of an electron-acceptor substituent attached to the double bond [33, 34].

α-Halo ethers add to the double bond in the presence of $ZnCl_2$ [35]. The adducts formed (66-93%) are evidently mixtures of stereoisomers.

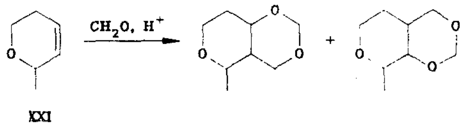


R, R^1=Alk, cycloalkyl, X=Cl, Br

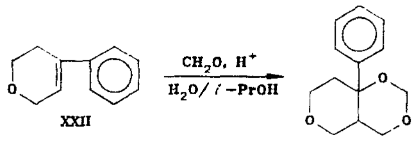
Dihydropyrans react with formaldehyde in an acidic medium via the Prins reaction [36] to give, usually, mixtures of products, the compositions of which depend on the reagent ratio. For example, cis-trans-diols XVIII predominate (53%) when XI:CH_2O = 1:2, whereas trioxadecalins XIX predominate (44%) when this ratio is 1:4. The yield of alcohol XX increases in the case of excess olefin (4:1) [37].



Dihydropyrans XI [13] and X [38] also react with CH_2O in acetic acid to give mixtures of mono- and diacetates but in low yields. Trioxadecalins of the XIX type are obtained as the principal reaction products in the reaction of XI with acetaldehyde; the trans isomer dominates (11:1) [37] in this case. A mixture of 6- and 9-methyl-1,3,7-trioxadecalin is formed in the reaction of 2-methyl-5,6-dihydropyran (XXI) with CH_2O in an overall yield of 42% [37].

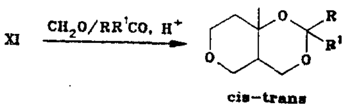


The isomer ratio (1:1) constitutes evidence for the equal likelihood of electrophilic attack at $C_{(3)}$ and $C_{(4)}$; this is also characteristic for other symmetrical olefins such as, for example, X [39]. Only cis-10-phenyl-1,3,7-trioxadecalin was isolated in the reaction of ether XXII with CH_2O [40].



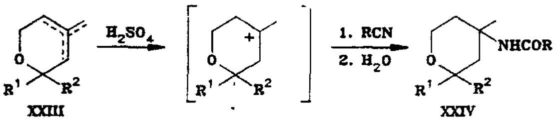
This result [illegible] the generally accepted carbonium-ion mechanism of the Prins reaction, but the authors' assumption that primarily cis-trans-diols are formed in analogy with dihydropyran XI was not proved experimentally.

Depending on the size of the substituents, the ratio of the cis-trans isomers changes from 1:11 ($R = H$, $R^1 = Me$) to 11:1 ($R = H$, $R^1 = C_6H_{13}$) or 8:1 ($R = C_5H_{11}$, $R^1 = Me$) in the reaction of XI with aliphatic aldehydes [41] and ketones [42] in the concerted Prins reaction.



The authors explain these results by means of the greater thermodynamic stabilities of cis-trioxadecalines, which exist in the form of two conformers, with an increase in the size of the substituents. The yields of acetals and ketals are, respectively, 12-58% and 5-20%.

The double bond in ethers XXIII was sufficiently active for these compounds to be able to participate in the Ritter reaction.

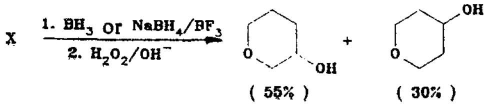


R^1, R^2=H, Alk or cycloalkyl ; R=Me, Ph, C_2H_3

The yields of the corresponding amides XXIV (45-65%) depend very little on the bulk of the substituents in the α position [43], although shielding of the heteroatom should facilitate protonation of the double bond and the formation of carbonium ions. This is evidently due to the fact that the reaction is realized under conditions of thermodynamic control. Similar results are also obtained when XI is used [44]. The yield of reaction products decreases to 30% when sulfuric acid is replaced by trifluoroacetic acid [43].

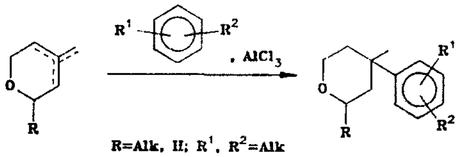
The acidic hydration of DHP evidently does not have preparative value, since the yields of the corresponding pyranol do not exceed 30% [45, 56]. 4-Methoxy-5,6-dihydropyran constitutes an exception, but the hemiketal that is formed in virtually quantitative yield in its hydrolysis is immediately converted to γ-pyrone [47].

Hydroboration makes it possible to obtain alcohols from olefins "counter" to the Markownikoff rule. The reaction proceeds unambiguously when there is a substituent such as an alkyl group attached to the double bond, as in the case of 2,4-dimethyl-5,6-dihydropyran [48]. Mixtures of isomeric pyranols are obtained in all of the remaining cases [2, 49].



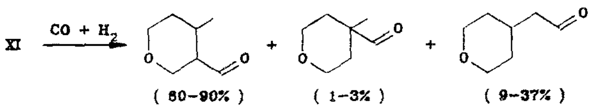
Ether XI reacts with acetic acid in the presence of a strongly acidic ion-exchange resin to give 4-acetoxy-4-methyltetrahydropyran [50].

Dihydropyrans readily alkylate aromatic compounds under the conditions of the Friedel–Crafts reaction (48-78%) [51].

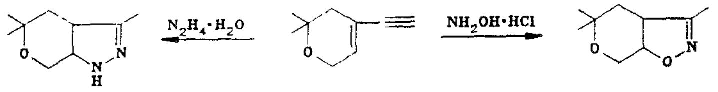


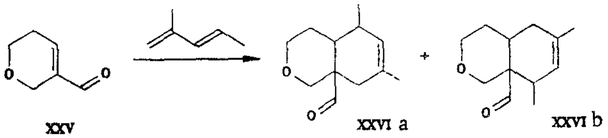
R=Alk, H; R^1, R^2=Alk

The hydroformylation of ether XI in the presence of an Rh catalyst leads to a mixture of products with preponderance of the expected 4-methyl-3-formyltetrahydropyran; the formation of 4-formylmethyltetrahydropyran is clearly due to prior isomerization of XI to 4-methylenetetrahydropyran [52].



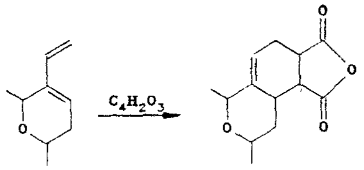
When a system of conjugated bonds is present in the DHP, they can be used to obtain new rings. For example, 2,2-dimethyl-4-ethynyl-3,6-dihydropyran reacts with hydrazine [53] and hydroxylamine [54] to give pyrazole and oxazole derivatives, while XXV reacts with 2-methyl-1,3-pentadiene to give adducts XXVIa and XXVIb via the scheme of the diene synthesis (68%) [55].





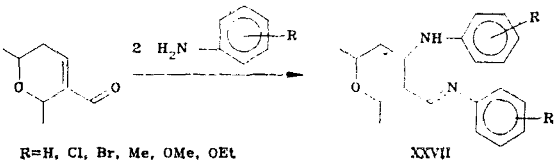
XXV XXVI a XXVI b

Such DHP can serve as the diene component, particularly in the reaction with maleic anhydride [56].



Intramolecular transformations are possible when other reaction centers are present in the DHP molecule. For example, dioxazoline derivatives (15-84%) were obtained when 6-trifluoromethyl-6-nitrodifluoromethyl-5,6-dihydropyrans were heated [57].

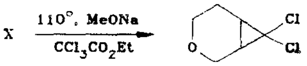
Independent reactions at two centers of the DHP are possible [58, 59]. Thus, imino amines XXVII were synthesized from crotonaldehyde dimer and arylamines.



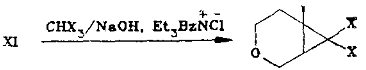
R=H, Cl, Br, Me, OMe, OEt

XXVII

The reactions of carbenes with DHP were first described ~20 years ago. The expected adduct of dichlorocarbene with dihydropyran X is formed in 25% yield [60].



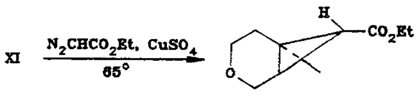
Dibromocarbene, generated in the CHBr$_3$—tert-BuOK system, gives better results in the reaction with ether XI (57%) [61]. The yield of products increases to 71-74% under conditions of interphase catalysis [62].



X=Cl, Br

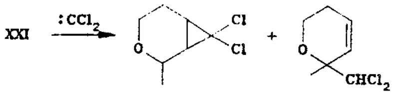
One might have expected the formation of cis and trans isomers in the reaction of XV with dichlorocarbene; however, one reaction product (78%) was obtained in [62]. The substituent in the allyl position evidently creates definite hindrance to attack by the carbene at the double bond. The formation of the trans isomer is preferable in this case.

The reaction of ether XI with carbethoxycarbene leads chiefly (83%) to exo-adduct XXVIII [61].



XXVIII

A very low yield of products is observed in the reaction of XI with methoxycarbene [61]; this is evidently due to the insufficient activity of the latter. A mixture of cis- and trans-7,7-dichloro-2-methyl-3-oxabicyclo[4.1.0]heptane and 2-dichloromethyl-2-methyl-5,6-dihydropyran in a ratio of 1:5.7:3.3 is obtained in the reaction of XXI with dichlorocarbene [63].

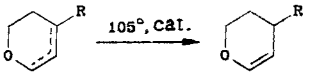


cis–trans

The formation of a product of insertion into the C–H bond is explained, in all likelihood, by prior coordination of dichlorocarbene at the heteroatom.

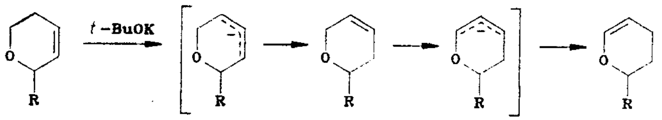
The isomerization of DHP includes reactions that are accompanied by migration of the double bond.

The percentage of ether XXIXa increases to 90% when an equimolar mixture of 5,6- and 3,4-dihydropyran is heated in a stream of nitrogen in the presence of the $RuCl_2(PPh_3)_3$ complex [64].



a R=H; b R=Me XXIX a,b

Ether XXIXb is formed in 92% yield from XI on the same catalyst at a higher temperature [65]. A mixture of $Fe(CO)_5$ and NaOH is a good isomerizing system. The yield of XXIXb reaches 90% based on converted ether XI at 180°C [66]. However, these results could not be reproduced later (59-65%) [67]. The isomerization of DHP can be realized in the presence of Ni_3As_2 under pressure with H_2 containing CO [68]. The CO and H_2 are evidently needed in this reaction for conversation of the catalyst to the active form (nickel carbonyls). Potassium tert-butoxide shifts the double bond in DHP to the vinyl position with high selectivity (89%), although the product is obtained in moderate yield (48%) [69]. Simply an excess amount of the base was also used for this sort of transformation, but the reaction took 5 h instead of 1 h [70]. The isomerization of 2-alkyl derivatives XXX proceeds very interestingly. It was found that chiefly vinyl ethers XXXb-d are formed as a result of a double anionotropic rearrangement through intermediate DHP XXXa.

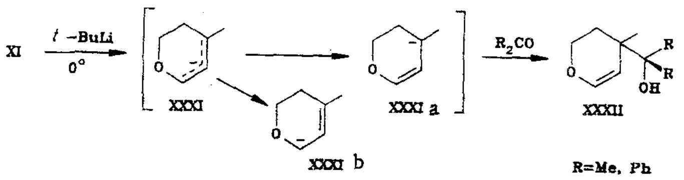


XXX XXX a XXX b-d

b R=Me (85%); c R=Et (80%); d R=Bu (18%)

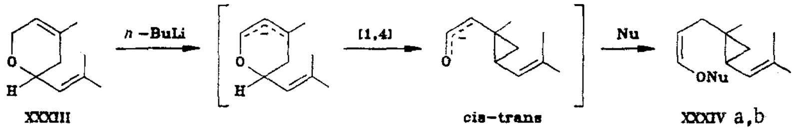
In the opinion of the authors, this is due to the effect of the donor properties of substituents R, which hinder the detachment of a proton from the 2 position of XXX [70].

The scheme of the formation of pyranols XXXII from ether XI also includes the prior rearrangement of allylic anion XXXI to XXXIa [71].



However, the low yield of pyranol XXXII (16%) and general considerations regarding the relative stabilities of carbanions XXXIa,b do not make it possible to regard the indicated reaction pathway as being the only possible pathway.

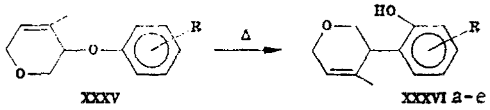
Carbanions of the allylic type are also formed by the action of n-BuLi on XXXIII. However, despite the milder reaction conditions (−27°C), the ring is cleaved as a result of [1, 4]-sigmatropic rearrangement of the DHP, and, when nucleophilic reagents (Ac_2O, Me_3SiCl) are added, this leads to mixtures of cis- and trans-cyclopropyl vinyl ethers XXXIVa,b (a:b = 3:2) in 60-80% yields.



The DHP ring is more stable when there is no substituent in the α position relative to the heteroatom, and a complex mixture of products due to both migration of the double bond in the ring and its cleavage is therefore formed from ether X under similar conditions [72].

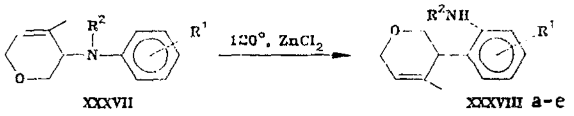
The isomerization conditions described in [70] proved to be unsuitable for ether XI (3%) and its pentamethylene derivative [67]. The conversion of XI on a calcium phosphate catalyst to an ether with exocyclic double bond – 4-methylenetetrahydropyran – also proceeds in very low yield [73].

Examples of the Claisen rearrangement of aryl ethers [74] and anilines [75] of the DHP series have been described. The rearrangement of ethers XXXV to the corresponding phenols XXXVIa-e is realized thermally by refluxing in N,N-dimethyl(or dibutyl)aniline [74].



a R=H; b R=NO_2; c R=*o*-Cl; d R=I; e R=*o,o*-di-Me

Anilines XXXVII also undergo smooth rearrangement when they are heated in nitrobenzene but only in the presence of $ZnCl_2$ as the catalyst [75].



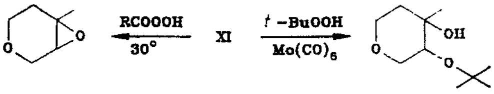
a $R^1=R^2=H$; b $R^1=Me$, $R^2=H$; c $R^1=$*o,o*-di-Me, $R^2=H$; d $R^1=H$, $R^2=Me$; e $R^1=H$, $R^2=Et$

In both cases the rearrangement occurs in the ortho position; if it is occupied, the rearrangement occurs in the para position (XXXVIIIc, XXXVIe).

On the whole, in reactions at the double bond DHP behave like other nucleophiles, but in a number of cases the presence of a heteroatom complicates the course of the reaction; this must be taken into account in planning syntheses with their participation.

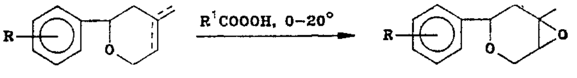
OXIDATIVE REACTIONS

In the case of the reaction of perbenzoic acid with olefins X and XI the Prilezhaev reaction leads to the expected epoxides in 66-77% yields [32]. The results are virtually the same when monoperphthalic acid is used, while the hydroperoxide oxidation of XI is accompanied by cleavage of the epoxide ring [13].



In contrast to XI, the reaction of ether XXI with monoperphthalic acid leads to a mixture of cis- and trans-2-methyl-3,4-epoxytetrahydropyran (13:87); the isomer ratio is virtually equalized (55:45) when perbenzoic acid is used [13]. Similar results were obtained in the epoxidation of XVII with perbenzoic [31] and m-chloroperbenzoic [30] acids.

In the reaction of mixtures of 2-aryl derivatives XXXIX with perbenzoic or monoperbenzoic acid epoxides XLa-d are formed only from the ethers with a double bond in the ring (42-50%) as a consequence of the considerably lower reactivities of the isomeric 2-aryl-4-methylenetetrahydropyrans [76].

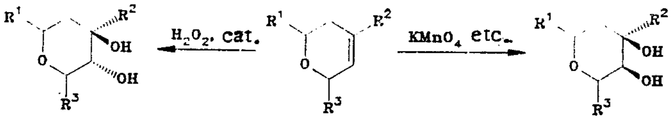


XXXIX a-d

XLa-d

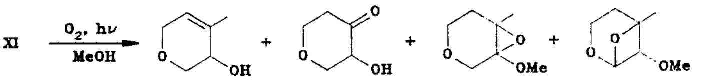
a R=H; b R=m-Br; c R=*o*-OH; d R=*p*-OMe

The hydroxylation of DHP can be carried out stereoselectively by varying the reaction conditions. Primarily the trans-diols are formed when H_2O_2 is used in the presence of catalysts (HCOOH, oxides, acids, or heavy metal salts) [77]. The use of reagents such as $KMnO_4$, H_2O_2—tert-BuOH, OsO_4—tert-BuOOH—acetone, and OsO_4—Py leads to the cis-diols [78].



Compound X [80], XI [77, 78], and 2,6-dimethyl- [79], 2,4 dimethyl- [81], and 2,4,6-trimethyl-5,6-dihydropyran [82] are oxidized by means of alkaline solutions of $KMnO_4$. The yields of cis-diols range from 14% to 62%. Better results were obtained when the OsO_4—Py system was used [78]. However, oxidation with $KMnO_4$ does not always stop at the step involving the formation of diols. For example, only a mixture of oxalic and acetic acids was obtained from 2,2,3,6,6-pentamethyl-5,6-dihydropyran [83]; this constitutes evidence for profound destruction of the molecule.

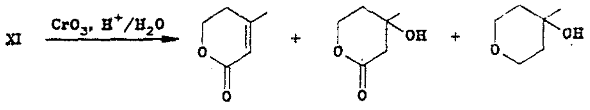
A number of studies have been devoted to the oxidation of olefins XI with oxygen in the presence of initiators and under irradiation. Hydroperoxides, which then are reduced by the usual methods, are formed in all cases. Unfortunately, the data on the oxidation of DHP are frequently contradictory; this is evidently explained by their patent character. For example, a mixture of pyranols XLI and XLII and epoxide XLIII was obtained in [84], while XLIV (exo:endo = 74:26) was obtained instead of XLIII in [85].



XLI XLII XLIII XLIV

Almost the same mixture of reaction products (XLI:XLII:XLIII = 27:14:58) is formed when initiators (Bz_2O_2, tert-BuOOH, etc.) are used [86]. In [87] it was noted that photooxidation leads only to pyranols XLI and XLII (75:25), while the reaction with azobisisobutyronitrile in MeOH leads to XLIV stereoisomers (4:1).

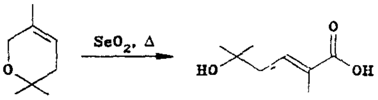
3-Methyl-2,4-pentadienal is formed in the oxidation of XI with the use of tetraphenylporphyrin complexes of cobalt. The reaction can be carried out in H_2O [88, 89] or in aliphatic alcohols [90]. Hemiacetals and acetals are obtained in the latter case. 6-Substituted 2-pyrones can be synthesized by photooxidation of the corresponding DHP in toluene [91]. Chromium compounds are often used as the oxidizing agents. Lactone XLV was obtained by means of tert-butyl chromite in CCl_4 or CrO_3 in sulfuric acid solution [92]. According to other data, a mixture of XLV, XLVI, and XLVII (8:62:30) in an overall yield of 32% is formed in the latter case [93].



XLV XLVI XLVII

Allylic oxidation with pyridine chlorochromate in CH_2Cl_2 proceeds more unambiguously. Thus, the corresponding 2-pyrones were obtained in 60-85% yields from X, XI, and 3-methyl·(ethyl)-3,6- and -5,6-dihydropyrans [94].

The oxidation of 2,2,5-trimethyl-3,6-dihydropyran with SeO_2 in aqueous dioxane is accompanied by ring opening (71%) [95].

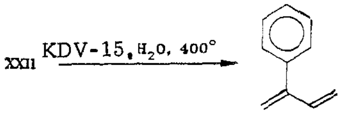


The oxidative reactions of DHP are evidently among the most interesting reactions in a synthetic respect, although their selectivity is often low.

REACTIONS WITH RING OPENING

Various reactions that are accompanied by opening of the DHP ring are known: thermal and catalytic reactions, reactions in the vapor and liquid phases, and reactions under the influence of acidic and basic agents.

The thermal degradation of DHP is usually considered to be a retrodiene reaction leading to the corresponding carbonyl compounds and dienes. Thus, CH_2O and isoprene are formed from XI [96], while acetaldehyde and piperylene are formed from 2,6-dimethyl-3,6-dihydropyran (XLVIII) [97]. Catalytic variants of this reaction with the use of silica gel [98, 99], aluminum silicate [100], and calcinated [101] or zeolite catalysts with various additives [102] are also known. A complex mixture of reaction products is formed in the pyrolysis (480-850°C) of the 3-formyl derivative of XLVIII [103]. When 3- and 5-propyl-3,6-dihydropyran are passed over Al_2O_3 (700-750°C), they give 1,3-heptadiene [104]. The degradation of XXII over a calcium phosphate catalyst is a good method for obtaining phenoprene (70%) [105].

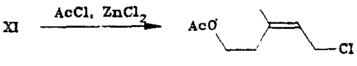


Cyclopentadienes (93-95%) are formed from X, XI, and XXI under the influence of H_3PO_4 (200-360°C) [106]. 1,3,5-Hexatriene can be obtained selectively (76%) from dihydropyran XXI when the catalyst is replaced by a less acidic one (silica gel) [107].

The reaction of ether XI with ammonia (400-600°C) in the presence of an aluminum silicate catalyst containing halogen and a metal oxide or sulfate leads to γ-picoline [108]. Pyridine can be obtained in a similar way [109] or on V_2O_5 (280-360°C) [110] from X. When 3-formyl-5,6-dihydropyran is passed over K, Sb, Al, or V oxides in a mixture with NH_3, it undergoes complex transformations, as a result of which 3-cyanopyridine (50%) is formed [111].

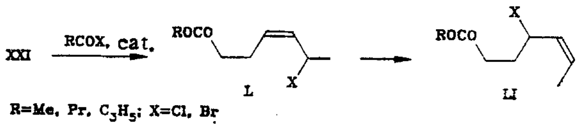
It is widely known that cyclic acetals and ethers are resistant to the action of aqueous solutions of alkalis. However, the isomeric DHP obtained from amylenes and formaldehyde undergo alkaline hydrolysis in the presence of an interphase catalyst, which leads to a mixture of C_{11} alkanols [112].

A number of studies have been devoted to the cleavage of DHP by acid halides. The important isoprenoid synthone XLIX was obtained by the action of acetyl chloride on XI in the presence of $ZnCl_2$ (60%) [113].



XLIX

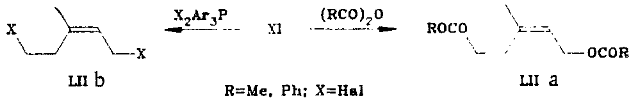
In the case of catalysis by $SnCl_4$ synthone XLIX is formed in high yield (90%) [114]. The reaction proceeds regioselectively, but with heating the cis isomer undergoes partial conversion to trans isomer [115]. Other acid halides such as acetyl bromide and benzoyl and propionyl chlorides can also be used for cleavage of the DHP ring [116, 117].



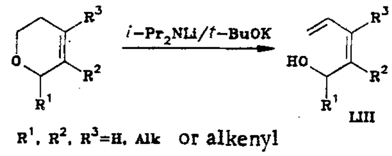
Two compounds with very close constants were isolated in the action of acetyl chloride on 2-acetoxymethyl-3,6-dihydropyran. Herault and Riobe [28] felt that they were isomers formed in the cleavage of the $O-C_{(2)}$ and $O-C_{(6)}$ bonds. Similar ring cleavage was assumed in the reaction of X with acetyl bromide [118]. Two compounds L and LI in a ratio of 1.2:1 to 2:1 (25-55%) were obtained by Ibatullin and coworkers [119] in a study of the reaction of ether XXI with a number of acid halides.

However, LI was found to be the product of allylic rearrangement of L. This means that the DHP ring is cleaved only at the $O-C_{(2)}$ bond under the influence of acid halides. The allyl isomer was evidently also isolated in [28].

The cleavage of XI by acid anhydrides under the influence of $ZnCl_2$ [120] and sulfuric, perchloric, or arenesulfonic acids [121], as well as triarylphosphine halides [122], leads to the expected compounds LIIa,b, which have, in all likelihood, primarily the Z configuration.

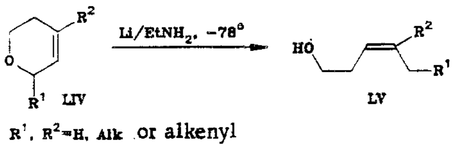


The reactions of DHP with basic agents are exceptionally valuable and useful in a synthetic respect. It has been pointed out that an intermediate carbanion of the allyl type, which then undergoes isomerization either simply with migration of the double bond or with ring cleavage, is formed by the action of bases on DHP. However, instead of isomerization, synchronous cleavage of the C—O bond and β elimination of a proton with the formation of dienic alcohols LIII (35-74%) occurs when the reaction is carried out under milder conditions (—40°C) with the use of lithium dialkylamides [123].

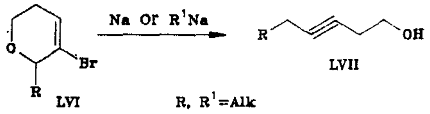


The synchronous mechanism of this reaction was demonstrated in the case of the cleavage of 6- and 2-ethyl-4-methyl-3,6-dihydropyrans [124]. It was found that the individual alcohols, rather than a mixture of them, which would be unavoidable in the case of the formation of the allyl carbanion, are obtained in this case. Other lithium alkylamides, particularly Et_2NLi [125], also evidently act similarly.

Cleavage of the DHP ring also occurs under the influence of Li in ethylamine, as demonstrated in the case of LIV but at the allylic C—O bond; unsaturated alcohols LV with a cis configuration (71-91%), including cis-3-hexen-1-ol, are formed stereoselectively in this case [126].



The reaction of 3-bromo derivatives LVI with Na or R^1Na is a good method for obtaining acetylenic alcohols LVII (64%) [127].



An analysis of the material set forth above shows that chief attention is being directed to the applied aspects of the chemistry of DHP and that there have been definite advances in this direction. However, the development of fundamental concepts will undoubtedly promote a fuller realization of the rich synthetic possibilities of this class of heterocycles.

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REACTION OF THE OXIDES OF SULFOLENE AND 1-METHYLCYCLOPENTENE WITH SODIUM AZIDE

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The oxides of sulfolene and 1-methylcyclopentene form the corresponding azidoalcohols with sodium azide. In the case of the methylcyclopentene oxide, the attack takes place primarily at the tertiary carbon atom.

It is known that the azide ion adds rather readily to either aliphatic or cyclic epoxides to form azidoalcohols [1-3]. There is no information in the literature concerning the reaction of oxides of the heterocyclic series with sodium azide. We showed previously that with all of the nucleophilic reactants studied, the structure and nature of the products of epoxide ring scission in epoxysulfolanes are determined by the α- or β-position of the sufonyl group with respect to the oxide ring [4, 5, 10]. It was of interest, therefore, to investigate the behavior of the epoxides of sulfolene and its methyl derivatives, I-III, in the reaction with sodium azide.

As the investigations showed, unsubstituted 3,4-epoxysulfolane (I) reacts with sodium azide in aqueous alcoholic solution in the presence of ammonium chloride to form addition product IV. In the IR spectrum of IV there is an absorption band 2125 cm^{-1} corresponding to the azido group and a hydroxyl group absorption band at 3415 cm^{-1}. The PMR spectrum of IV ($DMSO-d_6$) is analogous to that found in [4, 6], having lines in the 2.93-3.66 ppm region (two methylene groups), two proton multiplets at 4.33 ppm (3-H and 4-H), and also a doublet at 6.07 ppm (OH, J = 4 Hz) that disappears in dueteromethanol. This confirms that the structure of IV is 3-azido-4-hydroxysulfolane.

The action of sodium azide under analogous conditions and in the presence of mineral acids (H_2SO_4, H_3BO_3, $HClO_4$) on methyl substituted 3,4-epoxysulfolane (II) and 3-methyl-2,3-epoxysulfolane (III) did not lead to the formation of addition products. On brief heating, the initial epoxides escape and an increase in the reaction time leads to intense tar formation in the reaction mixture. A similar inertness toward azide ion was noted in the aliphatic, α,β-epoxysulfone series [7].

At the same time, the oxide of methylcyclopentene, V, which differs from oxide II by the absence of an SO_2 group in the ring, forms addition product VI when acted upon by sodium azide in aqueous solution in the presence of NH_4Cl. It is known that when sodium azide acts on saturated monoalkylepoxides, the azide ion attack is directed primarily, if not wholly,

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