Chemical Reactions of Spirooxiranes

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Abstract—The review covers the reactivity of spirooxiranes. The characteristic distinction of chemical behavior of this type epoxides from that of epoxycycloalkanes is discussed. In the spirooxiranes unlike epoxycycloalkanes the oxirane and alicyclic fragments are joined by one and not by two common atoms. The spirooxiranes are characterized by enhanced reactivity in the neutral and alkaline media, and also by versatile isomerizations and rearrangements in the presence of acidic catalysts. The relation between the chemical properties of spirooxiranes and the features of their electronic structure was considered. The main reactions of spirooxiranes with reductants, reactants with nucleophilic centers on oxygen, sulfur, carbon, nitrogen, and phosphorus, and with hydrogen halides are analyzed. The isomerization of spirooxiranes into carbonyl compounds and allyl alcohols is discussed. The possibility was considered of formation of the other cyclic systems proceeding from spirooxiranes.

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INTRODUCTION

Spirooxiranes are compounds with a three-membered oxygen-containing heterocycle joined to an alicyclic fragment by a common carbon atom. To this large group belong 1-oxaspiro[2.6]alkanes, in particular epoxides (1-6) [1-3], and also spirooxiranes with bicyclic (7a, b, 8) [4-7] and tetracyclic (9) fragments [4], unsaturated spirooxiranes (10a, b) [6], and bicyclospirooxiranes with more intricate structures [8-13].

Several spirooxiranes were synthesized with adamantane and other complicated carbon skeletons [14, 15].

![Chemical structures of spirooxiranes](image)
Also bispiroepoxides [16–21] and epoxides of this group with various heterocyclic fragments [22–24] were prepared. In some cases the spirooxiranes were isolated as individual spatial structures and optically active compounds [8, 25, 26].

The methods of synthesis for this group epoxides were described in a book [27], and before that in [28] and as some examples in reviews of general character [29, 30]. Besides the most often used peroxy acids also dioxiranes are now applied to the preparation of spirooxiranes [31]. An attempt to oxidize methylene-cycloalkanes in the presence of enzymes is known [32]. Since the double bond in methylene-cycloalkanes is less shielded by substituents than in cycloalkenes their epoxidation with peroxy acids and dioxiranes is of low stereoselectivity [29, 31, 33]. Therefore even in the modern procedures the synthesis of spirooxiranes with the desired stereostructure is carried out along the classical halohydrin method, e.g., in the synthesis of epicoryoline [33], in preparation of synthons for potential glycosyl transferase inhibitors [23] etc.

A group of new spirooxiranes (13) was recently obtained by [4+2]-cycloaddition of various dienophiles (enol ethers, substituted styrenes, N-methylvinylacetamide) to spirodienes (12) prepared by oxidation of substituted hydroxymethylphenols (11) by Adler–Beker procedure [34].

Under special conditions of diene synthesis was obtained spiroepoxide (15). The original strained oxaspiropentene (14) was first described in the same publication [35]. The structure of compound 14 was proved by comparison of parameters of its $^1$H and $^{13}$C NMR spectra with spectral parameters calculated by ab initio methods.

Epoxy ring is a structural moiety contained in quite a number of biologically active compounds, both natural and synthetic [30]. Among the biologically active epoxides are known numerous spirooxiranes prepared from natural terpenoids and the other natural substances of related structures. It is presumable that their active biological function is due to versatile transformations of the epoxides from this series. For instance, the alkylation of nucleophilic centers of polypeptide chains is known to be capable to alter the genetic code of a cell [36]. Therefore some epoxides are carcinogenous, and some others are used as antitumor pharmaceuticals. Some spirooxirane reactions serve as models for decoding of biological processes mechanism, and others are applied to development of syntheses of biologically active compounds or important synthons. These problems are treated in reviews [30] and in numerous special publications. Among spirooxanes are known antibiotics [30, 37–39], efficient growth inhibitors of arteries [40]. The derivatives of a sesquiterpene pentalenolactone among which quite a number was prepared by asymmetrical synthesis show versatile antibacterial and antiviral properties [37, 41, 42]. Fumagillin derivatives are successfully used in treatment of rheumatism, psoriasis, diabetes, and as antitumor agents [43].