Catalytic interaction of 1,3-diheteracycloalkanes with diazo compounds

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Abstract
The results are presented of research on the catalytic interactions of 1,3-diheteracycloalkanes with diazocompounds (N_2CH_2, N_2CHCO_2Me), the influence of the nature of the catalyst and structure of the starting heterocycles on the yield and structure of products formed.

Keywords: 1,3-Diheteracycloalkanes, diazo compounds, catalysis, 1,2-anionic rearrangement, cyclopropanation, carbene insertion into the C-X bond

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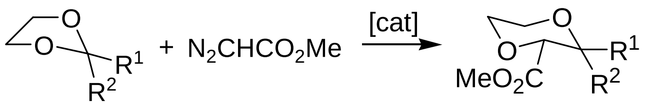
Introduction

In recent years, much attention has been focused on developing new regio- and stereoselective methods for the synthesis of 1,4-diheteracyclohexanes.[1–9] This is primarily due to high and various physiological activities of these heterocyclic compounds. For example, the morpholine fragment is involved as a structural element in many pharmacological drugs.[10] Tagetitoxin, containing the 1,4-oxathiane fragment is an RNA polymerase inhibitor.[11,12] Cyclopropanes containing the 1,3-dioxolane fragment are of interest as synthons for the synthesis of biologically active polyfunctional compounds,[13] for example, of 5,6-methanoleukotriene A_4, which is a stable and selective inhibitor of the biosynthesis of leukotriene.[14] as well as for the production of fragrance compounds for perfumery, such as (2*E*)-5-(2,2-dimethylcyclopropyl-3-methylpent-2-enal (citral-6,7-cyclopropane).[15]

One of the convenient procedures for the synthesis of 1,3-dioxane-, morpholine-, and oxathiane- derivatives is based on the intramolecular rearrangement of oxonium-, ammonium-, and sulfonium ylides, which in their turn are generated by the catalytic reactions of diazo compounds with 1,3-diheteracyclopentanes.[1,2,4,6,9,16] The goal of the present work is to study catalytic reactions of some 1,3-diheteracycloalkanes with N_2CH_2 and N_2CHCO_2Me and determine the regio- and stereoselectivity of this reaction.

Results and Discussion

Catalytic interaction of N_2CHCO_2Me with 1,3-diheteracycloalkanes. Earlier it has been shown that N_2CHCO_2Me reacts with acetals of furfural on the C-O or C-C bond depending on conditions.[17,18] We have studied interactions of mono-, di- and tri-substituted 1,3-dioxolane with methyl diazoacetate in the presence of $BF_3{\cdot}OEt_2$, $Cu(OTf)_2$, $CuSO_4$, $Rh_2(CF_3CO_2)_4$, $Rh(P(C_6H_5)_3)_3Cl$, CuCl and $Rh_2(OAc)_4$.[19] It is established that the interaction of 1,3-dioxolanes **1a-f** with N_2CHCO_2Me in the presence of 2 mol.% of $BF_3{\cdot}OEt_2$ has produced the corresponding 1,4-dioxanecarboxylates **2a-f** (the reaction time was 2 h). As a result of carbene introduction into the C(2)-O(1) bond of 2-mono- and 2,2-disubstituted-1,3-dioxolanes the expansion of dioxolane rings is observed (Scheme 1).



1 a-f **2 a-f**

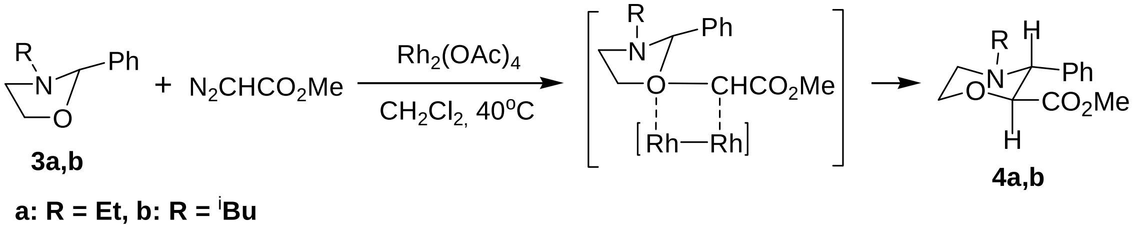
a: R^1 = H, R^2 = ^{i}Pr
b: R^1 = H, R^2 = Ph
c: R^1 + R^2 = $-(CH_2)_5-$
d: R^1 = Ph, R^2 = $CHBr_2$
e: R^1 = ^{i}Pr, R^2 = $CHCl_2$
f: R^1 = Ph, R^2 = $CHCl_2$

Scheme 1

2,2-Disubstituted-1,3-dioxolanes are mainly formed as *trans-* isomers under the conditions used by us.[19] The use of $Cu(OTf)_2$ or $CuSO_4$ as catalysts for carbene formation from methyl diazoacetate yields less satisfactory results. More strict conditions (70 °C) are required for carrying out the given reaction; and yet, the yield of the formed 1,4-dioxane **2a-f** does not exceed 13% and the basic products are dimethyl esters of maleic and fumaric acids.

In the reactions of 3-ethyl-2-phenyl- and 2,3-diphenyl- oxazolidines with methoxycarbonylcarbene, which is generated by thermocatalytic decomposition of methyl diazoacetate in the presence of copper bronze,[16] insertion occurred predominantly into the C-N bond of the oxazolidine ring to give morpholine-3-carboxylic acid esters. It was also noted[16] that in the presence of $Rh_2(OAc)_4$ neither insertion products of carbene into the C-N bond nor into the C-O bond are formed.

In the present study, we have examined the catalytic reactions of 3-alkyl-2-phenyl-1,3-oxazolidines (**3a,b**) and 2-phenyl-1,3-oxathiolane (**3c**) with N_2CHCO_2Me in the presence of $Rh_2(OAc)_4$. The reactions of oxazolidines **3a,b** with N_2CHCO_2Me in dichloromethane in the presence of 0.4 mol.% of the catalyst at 40 °C produced methyl 4-alkyl- 3- phenylmorpholine-2-carboxylates **4a** and **4b** in 50 and 46% yields, respectively (the reaction time was 2 h). In both cases, insertion of the carbene fragment into the C-O bond of the heterocycle occurs to give *trans*-isomers **4a,b** (Scheme 2).

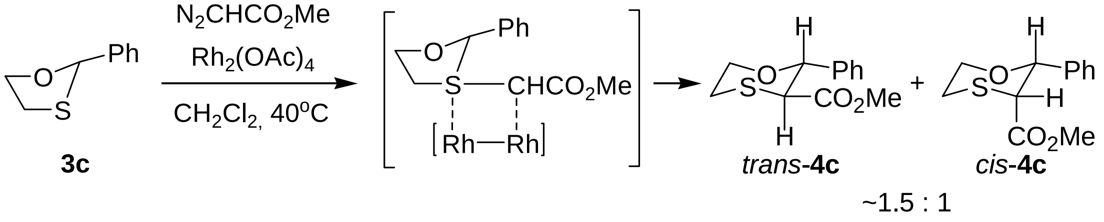


Scheme 2

The morpholine derivatives **4a,b** are generated apparently through the attack of methoxycarbonylcarbene on the oxygen atom of oxazolidines **3a,b** to form *O*-ylides, which undergo the Stevens rearrangement leading to ring enlargement.[20] It should be noted that thermocatalytic decomposition of N_2CHCO_2Me (120 °C, copper bronze) **[16]** with oxazolidine **1a** affords a complex mixture of compounds, in which the percentage of morpholine **4a** is lower than 13%.

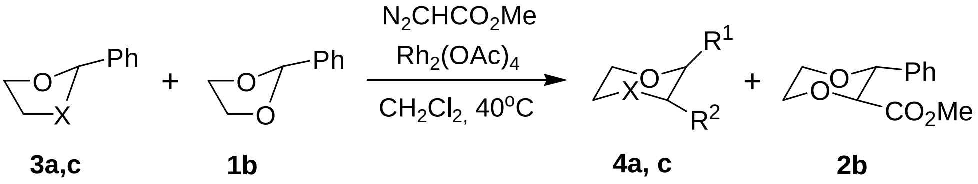
The stereochemical compositions of compounds **4a,b** were determined by analyzing the chemical shifts and spin-spin coupling constants in the ^1H NMR spectra. The ^1H NMR spectrum of compound **4a** shows doublets at δ 3.36 and 3.95 ($^3J_{2,3}$ = 8.9 Hz) corresponding to the methine protons at the C(3) and C(2) atoms, respectively, of the morpholine ring. The spin-spin coupling constant is indicative of the *trans* arrangement of the substituents at the adjacent carbon atoms. The COLOC 2D NMR spectrum of ester **4a** shows a cross-peak between the signal for the carbonyl carbon atom (δ 169.6) and a low-field signal for the methine proton at the C(2) atom (δ 3.95), which confirms that methoxycarbonylcarbene is inserted into the C(2)-O bond of oxazolidine **3a**.

The reaction of 2-phenyl-1,3-oxathiolane (**3c)** with N_2CHCO_2Me in CH_2Cl_2 in the presence of $Rh_2(OAc)_4$ produced methyl 2-phenyl-1,4-oxathiane-3-carboxylate (**4c**) in 72% yield (Scheme 3). In this case, as opposed to the reaction of 1,3-oxazolidines, the carbene fragment is inserted into the C-S bond of the heterocycle. Oxathiane **3c** being formed as a mixture of the *trans*- and *cis*-isomers in a ratio of 1.5 : 1. Earlier, it has been noted[21,22] that the reaction of ethyl diazoacetate with heterocycle **3c** proceeds in the presence of $Cu(acac)_2$ as well, but the corresponding *trans*- and *cis*-isomers of ethyl 2-phenyl-1,4-oxathiane-3-carboxylate were synthesized only in 19% yield (the isomer ratio was ~2 : 1).



Scheme 3

To reveal the relationships between the structure of 1,3-diheteracyclopentanes and the rate of insertion of methoxycarbonylcarbene into the carbon-heteroatom bond, the reactions of compounds **1b, 3a, 3c** with N_2CHCO_2Me in the presence of $Rh_2(OAc)_4$ were studied by the competitive reaction method (Scheme 4). The relative reactivity was determined at 40 °C by adding a solution of N_2CHCO_2Me in dichloromethane to a mixture containing dioxolane **1b** and its heteroanalog **3a** or **3c** in a molar ratio **1b**: **3a** (or **3c**): N_2CHCO_2Me: $Rh_2(OAc)_4$ = 250: 250: 100: 1.



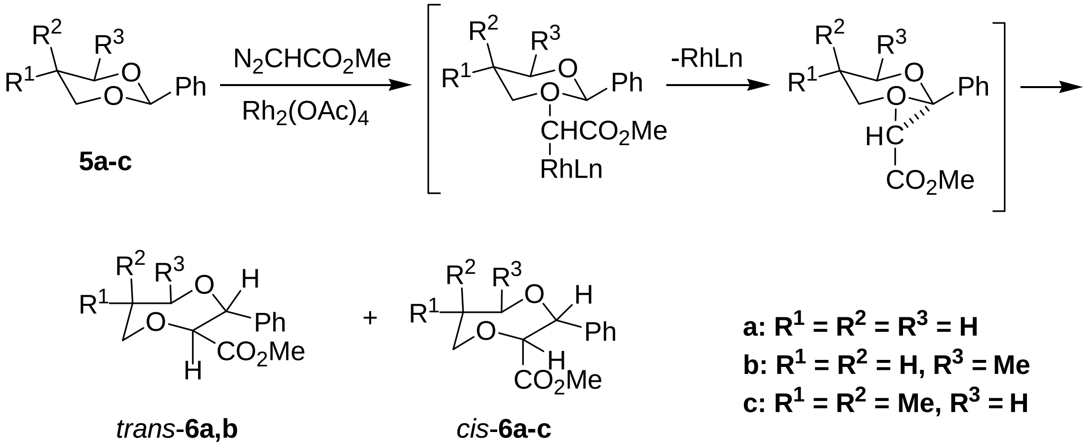
4a: X = NEt, R^1 = CO_2Me, R^2 = Ph
4c: X = S, R^1 = Ph, R^2 = CO_2Me

Scheme 4

As expected, 2-phenyl-1,3-oxathiolane **3c** showed the highest reactivity (k_{rel} (**3c/1b**) = 9.8), whereas oxazolidine **1a** appeared to be only just slightly more reactive than 1,3-dioxolane **1b** (k_{rel}**3a/1b**) = 1.7) although it is characterized by the insertion of the carbene fragment into the C-O bond rather than into the C-N bond. This fact is apparently attributed to the additional replacement at the nitrogen atom, which hinders the intermediate formation of *N*-ylide.

Catalytic reactions of diazo esters with 1,3-dioxanes, which are the homologs of 1,3-dioxolane, remain poorly studied, although some examples of Rh-catalyzed intramolecular transformations of 1,3-dioxanes derivatives of diazo esters and diazo ketones have been reported.[23] Therefore, catalytic interactions of 1,3-dioxanes (**5a-c**) with N_2CHCO_2Me in dichloromethane in the presence of 0.5 mol.% of $Rh_2(OAc)_4$ at 20 °C were investigated. The reaction results in 1,4-dioxepanes (**6a-c**) in 20, 40 and 46% yields, respectively. The individual *cis*- and *trans*-isomers of l,4-dioxepanes **6a-c** were isolated by column chromatography. It should be noted that the reaction mixture contained no product in which methoxycarbonylcarbene is inserted between the C(2) and O(3) atoms of dioxane **5b**. The resulting 1,4-dioxepanes **6a,b** consisted of mixtures of two stereoisomers with the *cis*-isomer (≥80%) being the major compound. However, dioxane **5c** reacts stereospecifically to give *cis*-6,6-dimethyl-2-methoxycarbonyl-3-phenyl-1,4-dioxepane (**6c**) in 46% yield (Scheme 5).

2-Unsubstituted and alkyl-containing 1,3-dioxanes (1,3-dioxane, 1,5-dioxaspiro-[5.5]-undecane and 4-methyl-, 2,2,4-trimethyl- and 2-isopropyl-4-methyl-1,3-dioxanes) did not react with methyl diazoacetate under our conditions.

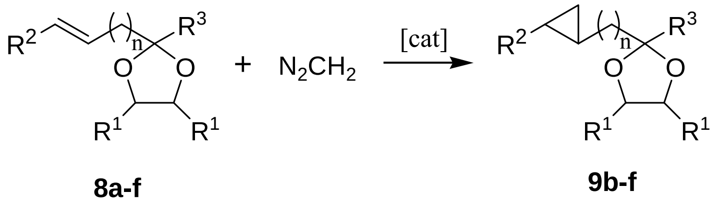


a: $R^1 = R^2 = R^3 = H$
b: $R^1 = R^2 = H, R^3 = Me$
c: $R^1 = R^2 = Me, R^3 = H$

Scheme 5

The possible mechanism of the reaction can include the generation of ylide followed by 1,2-anionic rearrangement (the Stevens rearrangement).[1,20] Apparently, the O(1) atom is involved in the formation of ylide; this is confirmed by the selective formation of products of formal insertion of methoxycarbonylcarbene into O(1)-C(2) bond. Successful reaction of methyl diazoacetate with benzaldehyde derivatives correlates well with the mechanism of 1,2-anionic rearrangement.[20] According to this mechanism, the migrating group in its transition state is a free radical stabilized by conjugation in its substituents, and thus the process occurs more easily.

Catalytic interaction of N_2CH_2 and N_2CHCO_2Me with unsaturated 1,3-diheteracycloalkanes. It has been demonstrated[24] that the introduction of the oxazolidine or boronate group into unsaturated compounds leads to an increase in both the yields of cyclopropanation products compared to those obtained in reactions with unfunctionalized molecules and the regioselectivity of cyclopropanation of dienes with N_2CH_2 in the presence of $Pd_2(OAc)_2$. The influence of the characteristics of the acetal substituents in olefins on catalytic reactions of the latter with N_2CH_2 has not been previously examined. In the present study, we examined the influence of the nature of the acetal group and the catalyst on the catalytic cyclopropanation with diazomethane of a series of unsaturated compounds, derived from *trans*-crotonaldehyde (**8a,d**), *trans*-cinnamaldehyde (**8b,e**) and hex-5-en-2-one (**8c,f**) (Scheme 6).



a: n = 0, $R^1 = R^3 = H, R^2 = Me$ **d: n = 0, $R^1 = CO_2Bu, R^2 = Me, R^3 = H$**
b: n = 0, $R^1 = R^3 = H, R^2 = Ph$ **e: n = 0, $R^1 = CO_2Bu, R^2 = Ph, R^3 = H$**
c: n = 2, $R^1 = R^2 = H, R^3 = Me$ **f: n = 2, $R^1 = CO_2Bu, R^2 = H, R^3 = Me$**

Scheme 6

Cyclopropanation was carried out at 5–10 °C by adding a solution of N_2CH_2 in Et_2O or CH_2Cl_2 to an unsaturated compound in the presence of a catalyst, in the molar ratio of 50: 150: 1 of olefin: N_2CH_2: catalyst, for 30 min. Investigation of cyclopropanation of dioxolane **8a** with the use of $Pd(OAc)_2$, $PdCl_2$, $Pd(acac)_2$, CuCl, $[CuOTf]_2 \cdot C_6H_6$, $Cu(acac)_2$, and $Cu(OTf)_2$, as the catalysts demonstrated that $Pd(acac)_2$ and $Cu(OTf)_2$ are the most efficient palladium and copper catalysts, respectively, under the reaction conditions used. Cyclopropanation catalyzed by $Pd(acac)_2$ or $Cu(OTf)_2$ afforded products in 99 and 49% yields, respectively. Hence, all further reactions were carried out with the use of these two catalysts. The resulting cyclopropanes were isolated by preparative TLC and characterized by ^{1}H- and ^{13}C- NMR spectroscopy.

Compound **8a** reacts with N_2CH_2 in the presence of $Pd(acac)_2$ or $Cu(OTf)_2$ to give a complex mixture of products. By contrast, cyclic acetal **8d** containing two electron-withdrawing butoxycarbonyl groups at positions 4 and 5 of the dioxolane fragment is readily subjected to cycloprotonation in the presence of $Pd(acac)_2$ to form dibutyl 2-(*trans*-2-methylcyclopropyl)-1,3-dioxolane-*trans*-4,5-dicarboxylate (**8d**). Unlike simple crotonaldehyde derivatives **8a**, cinnamaldehyde derivatives react with N_2CH_2 in the presence of $Pd(acac)_2$ to give the corresponding cyclopropane derivatives **9b,e** in high yields. Cyclopropanation of hexenone derivatives **8c,f** occurs with a somewhat higher efficiency compared to hexenone and produces cyclopropanes **9c,f** in 87-99% yields.

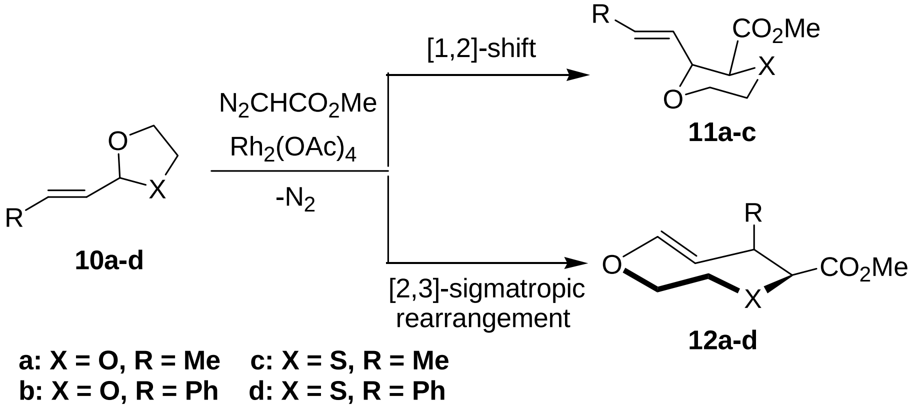
The $Cu(OTf)_2$ catalyst is less efficient than $Pd(acac)_2$ in cyclopropanation of cinnamaldehyde derivatives **8b,e** or hexenone derivatives **8c,f**, and these reactions give the corresponding cyclopropanes in low yields. In the reaction of unsaturated compound **8b**, $Cu(OTf)_2$ catalyzes the acetal deprotection giving rise to the starting cinnamaldehyde, the reaction being typical only of cinnamaldehyde derivatives.

The higher efficiency of Pd compounds in the cyclopropanation of unsaturated acetals is apparently associated with intramolecular stabilization of π -olefin complexes by oxygen atoms.[13b]

The study of catalytic cyclopropanation of 1,2-disubstituted double bonds in unsaturated carbonyl compounds and their acetal (ketal) derivatives with diazomethane provided evidence for higher selectivity of cyclopropanation of the latter compared to the starting unsaturated carbonyl compounds and for the activating effect of the acetal fragments on the reactivity of the C=C bond compared to the cyclopropanation of usual 1,2-disubstituted alkenes.[13b]

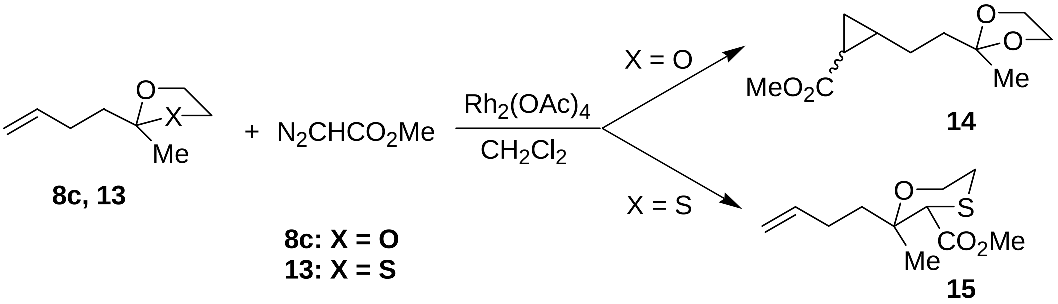
The interaction of equimolar quantities of methyl diazoacetate with cyclic acetals **10a,b** and 1,3-oxathiolanes **10c,d** in the presence $Rh_2(OAc)_4$ proceeds selectively and results in products of C-X insertion **11a-c** and [2,3]-sigmatropic rearrangement **12a-d** (Scheme 7). The absence of cycloaddition products of methoxycarbonylcarbene to the C=C bond in the reaction mixture and arrangement of substituents in the isolated products testifies that reaction proceeds through formation of one ylide. The formation of ylides takes place by the electrophilic addition of carbenoid species generated from methyl diazoacetate to the heteroatom under the action of the catalyst. The selectivity of formation of products of Stevens rearrangement **11a-c** and [2,3]-

sigmatropic rearrangement **12a-d** is defined by the influence of both electronic and steric factors of the substituents.[25,26]



Scheme 7

At the transition to 1,3-dioxo- and 1,3-oxathiolanes having a C=C bond in γ -position to a heterocyclic substituent, the regioselectivity of reactions with methyldiazoacetate is defined by the nature of the heteroatom. The reaction of 2-(but-3-enyl)-2-methyl-1,3-dioxolane **8c** with N$_2$CHCO$_2$Me leads to the formation of a mixture of dimethyl esters of *trans*- and *cis*-2-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]cyclopropanecarboxylic acids **14** in a 3 : 2 ratio and 40% total yield. At the same time, the reaction of 2-(but-3-enyl)-2-methyl-1,3-oxathiolane **13** with N$_2$CHCO$_2$Me catalyzed by Rh$_2$(OAc)$_4$ is accompanied by the insertion of a methoxycarbonylmethylene fragment into the five-membered ring resulting from the Stevens rearrangement of the initially formed *S*-ylide to give selectively methyl 2-(but-3-enyl)-2-methyl-1,4-oxathiane-3-carboxylate **15** in 50% yield (Scheme 8).



Scheme 8

Interaction of N$_2$CHCO$_2$Me with 2-(*trans*-2-phenylethynyl)- and 2-(but-3-enyl)-2-methyl-3-ethyl-1,3-oxazolidines in CH$_2$Cl$_2$ leads to formation of the corresponding unsaturated carbonyl compounds by catalyzed Rh$_2$(OAc)$_4$ cleavage of oxazolidines.

Conclusions

Convenient methods of synthesis of morpholines, 1,4-dioxanes, 1,4-oxathianes and 1,4-dioxepanes derivatives and 1,3-dioxolanes containing cyclopropane fragments are developed. They are based on the catalytic interactions of 1,3-diheteracycloalkanes with diazomethane and methyl diazoacetate. It is shown, that 1,3-dioxolanes react with N_2CHCO_2Me in the presence of $BF_3{\cdot}OEt_2$, $Cu(OTf)_2$, $CuSO_4$ or $Rh_2(OAc)_4$, leading to formation of 1,4-dioxanes, being the products of formal insertion of methoxycarbonylcarbene into the C(2)-O(1) bond. 1,4-Dioxepanes are synthesized by the interaction of N_2CHCO_2Me with 1,3-dioxanes in the presence of $Rh_2(OAc)_4$. Methoxycarbonylcarbene generated by the catalytic decomposition of methyl diazoacetate in the presence of $Rh_2(OAc)_4$, is regioselectively inserted into the C(2)-O bond of 3-alkyl-2-phenyl-1,3-oxazolidines and into the C(2)–S bond of 2-phenyl-1,3-oxathiolane. The activating effect of the acetal fragments on the reactivity of the C=C bond of unsaturated compounds in cyclopropanation with N_2CH_2 catalyzed by Cu and Pd compounds is shown. It is established, that cyclic acetals and 1,3-oxathiolanes react with methyl diazoacetate to yield the products of Stevens rearrangement and [2,3]-sigmatropic rearrangement.

Experimental Section

General Procedures. The ^1H- and ^{13}C- NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13 and 75.47 MHz, respectively) in $CDCl_3$ with $SiMe_4$ as the internal standard. The IR spectra were measured on a Specord M82-63 instrument in a thin layer. The mass spectra were obtained on an MX-1320 instrument; the ionizing electron energy was 70 eV; the temperature of the ionization chamber was 50-70 °C. The GLC analysis was carried out on a Chrom-5 chromatograph equipped with a flame ionization detector (with a 1200×5 mm column with 5% SE30 on Inerton N-AW DMCS (0.125-0.160 mm) using helium as the carrier gas. The TLC analysis was performed on Silufol chromatographic plates (Merck). Preparative separation was performed by column chromatography on silica gel Chemapol (60 L, 100/160 μm). Starting 1,3-diheteracycloalkanes were synthesized according to known procedures,[19,27] distilled under a stream of argon, and stored under an inert atmosphere over metallic sodium. The solvents (CH_2Cl_2, diethyl ether, benzene, hexane, and petroleum b.p. 40–70 °C) were purified according to standard procedures.

Reactions of 1,3-dioxolanes 1a-f with methyl diazoacetate in the presence $BF_3{\cdot}OEt_2$ (general procedure). Methyl diazoacetate 2.5 g (25 mmol) was added with vigorous stirring at 20 °C over 1 h to a solution of l,3-dioxolane (50 mmol) and $BF_3{\cdot}OEt_2$ 0.07 g (0.5 mmol). The reaction mixture was additionally stirred for 1 h. The residue was dissolved in 10 mL of diethyl ether and passed through a thin layer of Al_2O_3. All products **2a-f** were purified by vacuum distillation.

Methyl 3-isopropyl-1,4-dioxane-2-carboxylate (**2a**, 45%).[19] **Methyl 3-phenyl-1,4-dioxane-2-carboxylate** (**2b**, 89%).[19] **Methyl 3-cyclohexyl-1,4-dioxane-2-carboxylate** (**2c**, 30%).[19] **Methyl 3-(dibromomethyl)-3-phenyl-1,4-dioxane-2-carboxylate** (**2d**, 60%).[19] **Methyl 3-(dichloromethyl)-3-isopropyl-1,4-dioxane-2-carboxylate** (**2e**, 53%).[19] **Methyl 3-dichloromethyl-3-phenyl-1,4-dioxane-2-carboxylate** (**2f**, 82%).[19]

Reactions of 1,3-diheteracyclopentanes 3a–c with methyl diazoacetate. General procedure. A solution of methyl diazoacetate (1.10 g, 11 mmol) in CH_2Cl_2 (15 mL) was added to a stirred solution of 1,3-diheteracyclopentane (13 mmol) and $Rh_2(OAc)_4$ (24 mg, 0.054 mmol) in CH_2Cl_2 (35 mL) at 40 °C for 1 h. The reaction mixture was additionally stirred for 1 h. Then the solvent was removed, and the residue was dissolved in Et_2O (10 mL). The solution was passed through a thin layer of Al_2O_3, the solvent was removed *in vacuo*, and the residue was distilled off or chromatographed on silica gel.

Methyl *trans*-4-ethylmorpholine-3-phenyl-2-carboxylate (**4a**, 50%). [27a] **Methyl 4-isobutyl-3-phenylmorpholine-2-carboxylate** (**4b**, 46%). [27a] **Methyl 2-phenyl-1,4-oxathiane-3-carboxylate** (**4c** 72%).[27a]

Competitive reactions of methyl diazoacetate with 2-phenyl-1,3-dioxolane (1b) and 1,3-diheteracyclopentanes 3a and 3c. A solution of methyl diazoacetate (1 g, 10 mmol) in CH_2Cl_2 (15 mL; molar ratio **1b** : **3a** (or **3c**): N_2CHCO_2Me: $Rh_2(OAc)_4$ = 250: 250: 100: 1) was added to a stirred solution of dioxolane **1b** (3.77 g, 25 mmol), 1,3-oxazolidine **3a** (or **3c**) (25 mmol), and $Rh_2(OAc)_4$ (44.2 mg, 0.1 mmol) in CH_2Cl_2 (50 mL) at 40 °C for 2 h. After completion of the reaction, samples were withdrawn three times and GLC analysis was performed. The relative reactivities of 1,3-diheteracyclopentanes were calculated by the equation $k_{rel} = aS_1/S_0$, where S_0 is the peak area of methyl 3-phenyl-1,4-dioxane-2-carboxylate (**2b**), S_1 is the peak area of the insertion product of methoxycarbonylcarbene into the C-heteroatom bond of 1,3-diheteracyclopentane **3a** or **3b**, and a is the calibration factor (a = 1.14 and 1.08 for **4a** and **4c**, respectively). Based on the experimental data, k_{rel}(**3c/1b**) = 9.8 and k_{rel}(**3a/1b**) = 1.7.[27a]

Reactions of 1,3-dioxanes with methyl diazoacetate. General procedure. Methyl diazoacetate (1.12 g, 11.2 mmol) in 3 mL of CH_2Cl_2 was added with vigorous stirring at 20 °C over 1 h to a solution of l,3-dioxane (15 mmol) and $Rh_2(OAc)_4$ (0.03 g, 0.056 mmol) in 10 mL of CH_2Cl_2. One hour after, methylene chloride was evaporated, and the residue was dissolved in 10 mL of diethyl ether and passed through a thin layer of Al_2O_3. The solvent was removed, and the residue was chromatographed on silica gel in hexane-AcOEt with a gradient from 5 to 100% of AcOEt.

2-Methoxycarbonyl-3-phenyl-1,4-dioxepane (**6a**, 20%).[27b] **5-Methyl-2-methoxy-carbonyl-3-phenyl-1,4-dioxepane** (**6b**, 40%).[27b] ***cis*-6,6-Dimethyl-2-methoxycarbonyl-3-phenyl-1,4-dioxepane (6c**, 46%).[27b]

Cyclopropanation of unsaturated 1,3-dioxolanes. General procedure. A 0.45*M* N_2CH_2 solution in Et_2O (45 mL) was added with stirring to a solution of 1,3-dioxolane (7.0 mmol) and Pd(acac)$_2$ (0.042 g, 0.14 mmol) in Et_2O (20 mL) (or Cu(OTf)$_2$ (0.051 g, 0.14 mmol) in CH_2Cl_2 (20 mL)) at 5-10 °C for 30 min. The reaction mixture was additionally stirred for 30-40 min and passed through a thin layer of Al_2O_3. The solvent was removed in low vacuum. The residue was distilled or chromatographed on SiO_2.

2-(*trans*-2-Phenylcyclopropyl)-1,3-dioxolane (**9b**, 98%).[27c] **2-(2-Cyclo-propylethyl)- 2-methyl-1,3-dioxolane** (**9c**, 87%).[27c] **Dibutyl 2-(*trans*-2-methylcyclopropyl)-1,3-dioxolane-*trans*-4,5-dicarboxylate** (**9d**, 95%).[27c] **Dibutyl 2-(*trans*-2-phenylcyclopropyl)-1,3-dioxolane-*trans*-4,5-dicarboxylate** (**9e**, 99%).[27c] **Dibutyl 2-(2-cyclopropropylethyl)-2-methyl-1,3-dioxolane-*trans*-4,5-dicarboxylate** (**9f**, 99%).[27c]

Catalytic reaction of 2-alkenyl-1,3-diheteracyclopentanes with methyl diazoacetate. General procedure. Methyl diazoacetate (0.7 g, 7.0 mmol) in 20 mL of CH_2Cl_2 was added to a solution of 7.0 mmol of an unsaturated compound (**10a-d, 8c, 13**) and 0.07 mmol of $Rh_2(OAc)_4$ in 10 mL of the solvent over 1 h and the mixture was stirred additionally for 1–1.5 h with heating. The solvent was removed, the residue was dissolved in 10 mL of diethyl ether and passed through a thin layer of Al_2O_3, the solvent was removed under slightly reduced pressure, and the residue was distilled in vacuum or chromatographed on SiO_2.

Methyl 3-(*trans*-prop-1-enyl)-1,4-dioxane-2-carboxylate (**11a**, 32%).[27d] **Methyl 3-(*trans*-2-phenylvinyl)-1,4-dioxane-2-carboxylate** (**11b**, 47%).[27d] **Methyl 3-(*trans*-prop-1-enyl)-1,4-oxathiane-2-carboxylate** (**11c**, 8%).[27d] **Methyl 6-methyl-2,3,5,6-tetrahydro-1,4-dioxocyne-5-carboxylate** (**12a**, 55%).[27d] **Methyl 6-phenyl-2,3,5,6-tetrahydro-1,4-dioxocyne-5-carboxylate** (**12b**, 23%).[27d] **Methyl 6-methyl -2,3,5,6-tetrahydro-1,4-oxathiocyne-5- carboxylate** (**12c**, 10%).[27d] **Methyl 6-phenyl-2,3,5,6-tetrahydro-1,4-oxathiocyne-5-carboxylate** (**12d**, 10%).[27d] **Methyl 2-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]-cyclopropanecarboxylate** (**14**, 87%).[27d] **Methyl 2-(but-3-enyl)-2-methyl-1,4-oxathiane-3-carboxylate** (**15**, 50%).[27d]

References and Footnotes

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