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Catalyst development for the synthesis of ozonides and tetraoxanes under heterogeneous conditions. Disclosure of an unprecedented class of fungicides for agricultural application

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Abstract: The catalyst $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$ supported on SiO_2 was developed for peroxidation of 1,3- and 1,5-diketones with hydrogen peroxide with the formation of bridged 1,2,4,5-tetraoxanes and bridged 1,2,4-trioxolanes (ozonides) with high yield based on isolated product (up to 86 and 90% respectively) under heterogeneous conditions. Synthesis of peroxides under heterogeneous conditions is a rare process and represents a challenge for this field of chemistry, because on a surface of the catalyst peroxides tend to decompose. A new class of antifungal agents for crop protection, cyclic peroxides: bridged 1,2,4,5-tetraoxanes and bridged ozonides, was discovered. Some ozonides and tetraoxanes exhibit a very high antifungal activity and are superior to commercial agro fungicides such as Triadimefon and Kresoxim-methyl. It is important to note that none of the agro fungicides used in agricultural chemistry contains peroxide fragment.

Introduction

Organic peroxides are important class of compounds for the development of drugs on their basis. Significant progress in medicinal chemistry of peroxides achieved in the development of drugs for the treatment of malaria.[1] Artemisinin and its derivatives (Artemether, Arteether, Artesunate) for the past two decades are used to treat malaria. In 2015, the Nobel Prize in Medicine was awarded to Youyou Tu for the discovery and development of Artemisinin, a natural peroxide antimalarial drug.[2] In 2012, the first commercial antimalarial drug was developed on the basis of synthetic ozonide Arterolane. Organic peroxides in addition to antimalarial activity possess a high anthelmintic[3] and anticancer[4] activity. Cyclic peroxides demonstrate anti-tuberculosis,[5] antiviral,[6] fungicidal,[3g] and plant growth regulatory activity.[7] However, until this work, organic peroxides had never been considered as crop protection agents.

The key reagents in the synthesis of organic peroxides are mainly ketones and aldehydes due to their availability and ease of reaction between the carbon atom of the carbonyl group and the highly nucleophilic oxygen atom of the peroxidizing agent. Peroxidation of ketones with hydrogen peroxide opened access to the synthesis of various classes of peroxides, such as geminal bis-peroxides,[8] geminal bis-hydroperoxides,[9] β-hydroxy-hydroperoxides,[10] tetraoxanes,[11] cyclic triperoxides,[12] tricyclic monoperoxides.[13] The peroxidation of monoketones and their derivatives has been studied in detail.[1g, 8b, 9e, 9f, 14] Peroxidation of diketones was studied much less,[11f, 15] which was associated with the formation of complex mixtures of inseparable peroxide products. For this reason, the selective synthesis of peroxides on the basis of diketones is a very difficult task. We have found that selective synthesis of peroxides can be carried out via peroxidation of β-diketones catalyzed by strong acids (H_2SO_4, $HClO_4$, HBF_4, and $BF_3{\cdot}Et_2O$) and heteropolyacids (phosphomolybdic, phosphotungstic).[11a, 11c] Peroxidation of β, δ'-triketones employing heteropolyacids as a catalyst leads to the formation of bridged keto-tetraoxanes, bridged keto-ozonides and tricyclic monoperoxides.[13a, 13b] Unfortunately, this method suffers from structural limitation, peroxidation occurs only if β,δ'-triketones bear a benzylic substituent in the α-position. In the case of any other substituent only tricyclic monoperoxides are formed. Recently, we developed an ozone-free approach to the synthesis of bridged 1,2,4-trioxolanes (bridged ozonides) from 1,5-diketones and H_2O_2 under homogeneous conditions.[16] Generally all known ozonides are synthesized by ozonolysis of alkenes[17] or by the reaction of *O*-methyl oximes with a carbonyl compound in the presence of ozone.[18] In the literature, there are only a few examples of the synthesis of ozonides from carbonyl compounds and hydrogen peroxide.[5c, 9f, 19]

Generally, the peroxidation of carbonyl compounds is carried out under homogeneous conditions. On the contrary, under heterogeneous conditions on the surface of the catalyst,

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peroxides, including hydrogen peroxide, tend to decompose.[20] There are only a few syntheses of peroxides under heterogeneous conditions proposed for more than a century: heminal bis-hydroperoxides,[14q, 21] β-hydroxy-hydroperoxides,[22] 1,2,4-trioxanes,[23] peroxides from β dicarbonyl compounds,[24] and β,δ'-triketones.[13b]

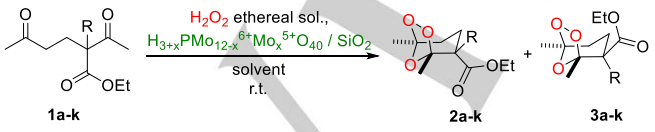
This work discloses a methodology for the selective peroxidation of 1,3- and 1,5-diketones under heterogeneous conditions. Phosphomolybdic acid (PMA) was chosen as a catalyst. PMA is able, when interacting with H_2O_2, to form peroxo-complexes with the -Mo-O-O- fragment.[25] However, taking into account that the PMA/H_2O_2 system oxidizes alkenes,[25i, 26] alcohols,[27] and dicarbonyl compounds, the result of the peroxidation of 1,3- and 1,5-diketones under heterogeneous conditions is *a priopi* unpredictable and not obvious. We have chosen SiO_2 as a support for the PMA, since it is one of the most convenient and available materials for various promotion and catalytic systems.[28]

In this study, we succeeded to develop a mixed valence PMA catalyst ($H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$) supported on SiO_2, which allows to carry out the peroxidation of 1,3- and 1,5-diketones with the selective formation of 1,2,4,5-bridged tetraoxanes and bridged ozonides. To the best of our knowledge, the ozone-free synthesis of ozonides under heterogeneous conditions was developed for the first time.

Another important achievement of this work is the discovery of a new class of fungicides for crop protection - cyclic peroxides. This finding was practically unpredictable, because none of the fungicides utilized in agrochemistry contained a peroxide moiety. Synthesized in this work ozonides and tetraoxane exhibit a very high fungicidal activity against phytopathogenic fungi and exceed widely used agrochemical fungicides such as Triadimefon and Kresoxim-methyl.

Results and Discussion

The peroxidation of 1,5-diketones **1a-k** with an ethereal solution of H_2O_2 under the action of a mixed valence PMA catalyst ($H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$) supported on SiO_2 in the presence solvents as toluene, benzene, CCl_4, CH_2Cl_2, Et_2O selectively produces stereoisomeric ozonides **2a-k** and **3a-k** (Scheme 1).

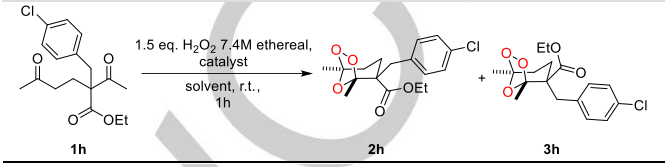


a: R = H; **b:** R = Et; **c:** R = Bu^n; **d:** R = Hex^n; **e:** R = $CH_2CH{=}CH_2$; **f:** R = CH_2CH_2CN; **g:** R = $CH_2CH_2C(O)OEt$; **h:** R = 4-$ClC_6H_4CH_2$; **i:** R = 3-$ClC_6H_4CH_2$; **j:** R = 4-$FC_6H_4CH_2$; **k:** R = 3-$MeOC_6H_4CH_2$;

Scheme 1. Synthesis of stereoisomeric ozonides **2a-k** and **3a-k** from 1,5-diketones **1a-k**.

The peroxidation of ethyl 2-acetyl-2-(4-chlorobenzyl)-5-oxohexanoate **1h** was used to study an effect of the type of treatment and deposition of PMA ($H_3PMo_{12}O_{40}{\times}H_2O$) on the SiO_2 surface (Fig. 1), the amount of H_2O_2, the duration of peroxidation, the amount of catalyst, the ratio of PMA:SiO_2, and the nature of a solvent on the yield of stereoisomeric ozonides **2h** and **3h** (Table 1). The source of H_2O_2 was a 7.4M solution of H_2O_2 in Et_2O. Toluene, benzene, CCl_4, CH_2Cl_2, Et_2O were chosen as solvents because PMA does not dissolve in them.

Table 1. Synthesis of ozonides **2h** and **3h** from 1,5-diketone **1h** and H_2O_2[a]



Entry	Catalyst	Solvent	Weight % PMA in PMA/SiO_2	Molar ratio PMA / **1h**	Isolated yield **2h**+**3h**, %	**2h**:**3h**[b] Ratio
1	PMA	Toluene	-	0.05	traces	-
2	PMA-**(A)**	Toluene	-	0.05	50	0.72:1.0
3	PMA-**(B)**	Toluene	-	0.05	72	1.13:1.0
4	PMA-**(C)**	Toluene	-	0.05	18	0.64:1.0
5	PMA/SiO_2 -**(D)**	Toluene	10	0.05	26	0.70:1.0
6	PMA/SiO_2 -**(E)**	Toluene	10	0.05	90 (57)[c]	0.87:1.0
7	PMA/SiO_2 -**(E)**	Toluene	10	0.01	8	1.0:1.0
8	PMA/SiO_2 -**(E)**	Toluene	10	0.03	65	0.91:1.0
9	PMA/SiO_2 -**(E)**	Toluene	10	0.10	94	0.97:1.0
10	PMA/SiO_2 -**(E)**	Toluene	10	0.15	95	1.70:1.0
11[d]	PMA/SiO_2 -**(E)**	Toluene	10	0.05	61	0.84:1.0
12[e]	PMA/SiO_2 -**(E)**	Toluene	10	0.05	79	0.77:1.0
13[f]	PMA/SiO_2 -**(E)**	Toluene	10	0.05	77	0.75:1.0
14[g]	PMA/SiO_2 -**(E)**	Toluene	10	0.05	93	0.93:1.0
15	PMA/SiO_2 -**(E)**	Benzene	10	0.05	60	0.66:1.0
16	PMA/SiO_2 -**(E)**	CCl_4	10	0.05	71	0.73:1.0
17	PMA/SiO_2 -**(E)**	CH_2Cl_2	10	0.05	82	1.27:1.0
18	PMA/SiO_2 -**(E)**	Et_2O	10	0.05	66	0.65:1.0
19	PMA/SiO_2 -**(F)**	Toluene	20	0.05	80	0.80:1.0
20	PMA/SiO_2 -**(F)**	Toluene	20	0.10	95	1.10:1.0
21	PMA/SiO_2 -**(G)**	Toluene	30	0.05	85	0.95:1.0
22	PMA/SiO_2 -**(G)**	Toluene	30	0.10	95	1.38:1.0
23	PMA/SiO_2 -**(G)**	Toluene	30	0.15	95 (92)[c]	3.27:1.0

[a] A 7.4 M ethereal solution of H_2O_2 (1.0 – 3.0 mol H_2O_2 / 1.0 mol of 1,5-diketone **1h**) and PMA (0.105g, 0.046 mmol of $H_3PMo_{12}O_{40}$), PMA-**(A-C)** (0.084 g, 0.046 mmol of $H_3PMo_{12}O_{40}$) or PMA/SiO_2-**(D-G)** (0.01-0.15 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,5-diketone **1h**) were successively added to a stirred

solution of 1,5-diketone **1h** (0.300 g; 0.92 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1h (Procedures for the preparation of catalysts PMA-**(A-C)** and PMA/SiO_2-**(D-G)**, see the Supporting Information).

[b] The ratio of ozonides **2h**:**3h** was determined by the ^{1}H NMR spectroscopic data.

[c] Scaled to 1.0 gram of 1,5-diketone **1h**

[d] Molar ratio H_2O_2 : **1h** = 1.0 : 1.0

[e] Molar ratio H_2O_2 : **1h** = 3.0 : 1.0

[f] The reaction mixture was stirred at 20-25°C for 0.5h

[g] The reaction mixture was stirred at 20-25°C for 24h

The peroxidation of diketone **1h** in toluene for 1 hour at room temperature using commercial yellow crystalline solid of PMA ($H_3PMo_{12}O_{40}\times H_2O$, where the amount of water can reach 30 molecules per molecule of the acid[29]) and a molar ratio of H_2O_2 : PMA : diketone = 1.5 : 0.05 : 1.0 produces target ozonides **2h** and **3h** only in trace amounts (Run 1, Table 1).

According to the literature, crystallization water eliminates from PMA at 150 °C.[30] We carried out TGA analysis of a bulk PMA used in the present work. The results showed, that upon reaching 150 °C the crystallization water is completely eliminated. There is no significant change in weight in the temperature range of 150-800 °C, which indicates about formation of anhydrous PMA (See SI). Based on these results, we carried out heat treatment of PMA at 150 °C in air atmosphere for two hours at atmospheric pressure. This catalyst PMA-(**A**) allowed to obtain target ozonides with a yield up to 50% on isolated product with ratio **2h** : **3h** = 0.72: 1.0 (Run 2, Table 1). The ratio of ozonides **2h** : **3h** was determined by the ^{1}H NMR spectroscopic data (for ozonide **2h**, the characteristic peaks in the ^{1}H NMR spectrum include singlets at 1.48 ppm (s, 3H, C***H***$_3$CCH$_2$) and 1.79 ppm (s, 3H, C***H***$_3$CC) whereas for ozonide **3h**, they include singlets at 1.56 ppm (s, 3H, C***H***$_3$CCH$_2$) and 1.66 ppm (s, 3H, C***H***$_3$CC). The characteristic NMR spectral features of **2** and **3** compound series were carefully described in our previous papers[16a,b]. Then we decided to carry out stepwise heating of PMA to 150 °C, first at 40 °C for 30 min., then at 60 °C - 30 min.; at 80 °C - 30 min.; at 100 °C - 30 min.; and then at 150 ° C for one hour. Thus PMA-(**B**) was prepared which permitted to obtain target products with yield up to 72% with ratio **2h** : **3h** = 1.13 : 1.0 (Run 3, Table 1). Probably, in the case of stepwise heating of PMA, the layer-by-layer elimination of crystallization water leads to formation of more accessible active catalytic sites than in case of PMA-(**A**) preparation. In order to facilitate the elimination of water, $H_3PMo_{12}O_{40}\times H_2O$ had been dissolved in ethanol and then the solvent was evaporated at 150 °C and 1 atm. of air, and the resulting residue was heated additionally at 150 °C for 1 hour. Obtained catalyst PMA-**(C)** was

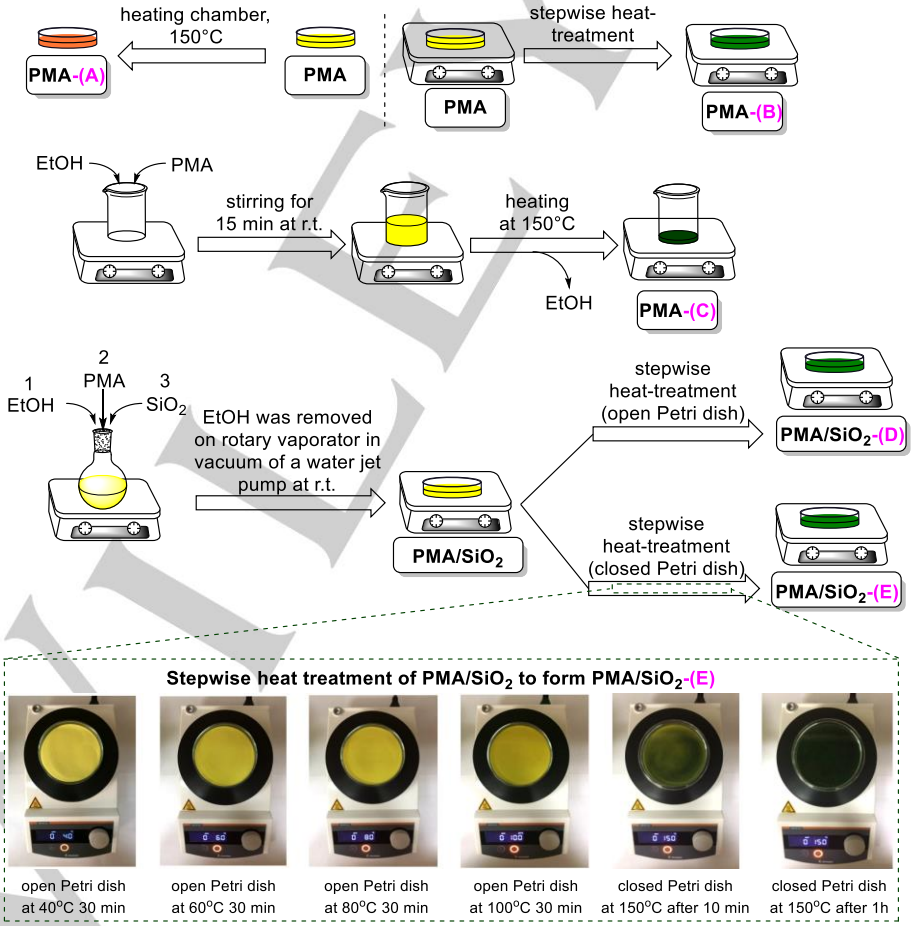


Figure 1. Procedures for the preparation of catalysts PMA-**(A-C)**, PMA/SiO_2, and PMA/SiO_2-**(D-G)** for the synthesis of ozonides. A more detailed description of the techniques presented in SI.

applied for the peroxidation of diketone **1h**, but the yield of the target ozonides was only 18% (Run 3, Table 1). The data of the Raman spectroscopy of PMA-**(C)** showed that during the preparation of this catalyst, the Keggin structure of PMA was destroyed with the formation of orthorhombic α-MoO_3 (Fig. 2). Raman spectroscopy is a well-known technique to investigate supported and unsupported Keggin structures of heteropolyacids.[31] Pure bulk PMA shows Raman bands at 990 cm^{-1} and 979 cm^{-1}, which can be assigned to the symmetric and asymmetric stretching vibration of terminal Mo=O_t, respectively, and less intense bands at 877 cm^{-1} (ν_{as} Mo–Ob–Mo) and 593 cm^{-1} (ν_s Mo–Oc–Mo).[27a] The Raman spectra of PMA-**C** differ from the spectra of the pure bulk PMA and the band at 815 cm^{-1} becomes the most intensive (Fig. 2). The observed bands position at 990 cm^{-1}, 815 cm^{-1}, and 661 cm^{-1} and intensity ratio are very close to Raman spectra of orthorombic molybdenum oxide − α-MoO_3 observed earlier[31-32] with maxima at 995, 820 and 666 cm^{-1}. From the technological point of view, the use of PMA-**(B)** was inconvenient due to unequal spreading of PMA-**(B)** on the glass walls of the flask, and difficulties with its regeneration.

At the next stage, we decided to deposit commercial PMA ($H_3PMo_{12}O_{40}\times H_2O$) on commercial silica gel SiO_2 60 Å (0,060-0,200 mm, S=470-530 m^2/g) in the amount of 10 wt.%. For this, PMA was dissolved in EtOH and SiO_2 was added with stirring, then the suspension was stirred for 15 min., and the solvent was evaporated on a rotary evaporator under vacuum of water jet pump at 30 °C. Then, the resulting PMA/SiO_2 was transferred to a Petri Dish without a lid and was heated as in the case of the preparation of PMA-**(B)**. Obtained catalyst PMA/SiO_2-**(D)** was applied for the peroxidation of diketone **1h**, but the yield of ozonides **2h** and **3h** on isolated product was only 26% (Run 5, Table 1). To our surprise it turned out that when preparing the catalyst PMA/SiO_2-**(D)**, it was found that covering a Petri Dish with a Petri Dish lid after reaching 150 °C led to the formation of a more efficient catalyst PMA/SiO_2-**(E)**. Using PMA/SiO_2-**(E)**, the target ozonides **2h** and **3h** were synthesized with a yield of 90% (run 6, table 1).

Preparation of PMA/SiO_2-**(E)** with covered Petri Dish, on the one hand, led to incomplete removal of water from a sample. On the other hand, this procedure favors the retention of ethanol vapor, the interaction of Mo^{6+} with which led to the partial reduction of Mo^{6+} to Mo^{5+}. It is known that the Keggin anion of PMA in the presence of reducing agent, including ethanol, can be reduced.[30a, 30b, 33] This leads to formation negatively charged reduced PMA and accompanies by a color change from yellow to blue or green converting heteropolyanions to so-called heteropoly blues.[22a, 27a, 33b, 34] It is believed that protons are attached to this reduced anion to compensate the resulting excess of negative charges.[33a, 35] Indeed as can see from Fig. 1 the color of PMA/SiO_2-**(E)** sample changes from yellow to dark green, and when hydrogen peroxide is added to PMA/SiO_2-**(E)**, the color changes from green to yellow.

The data of Raman spectroscopy show (Fig. 2), that in the case of PMA/SiO_2-**(E)** we can see Raman narrow band at 1011cm^{-1} which corresponds to the stretching vibration of terminal Mo=O of PMA and broad Raman band with maximum at 825cm^{-1}, which might be assigned to molybdenum oxide mixtures of orthorhombic α-MoO_3 and monoclinic β-MoO_3 phases.[31b]

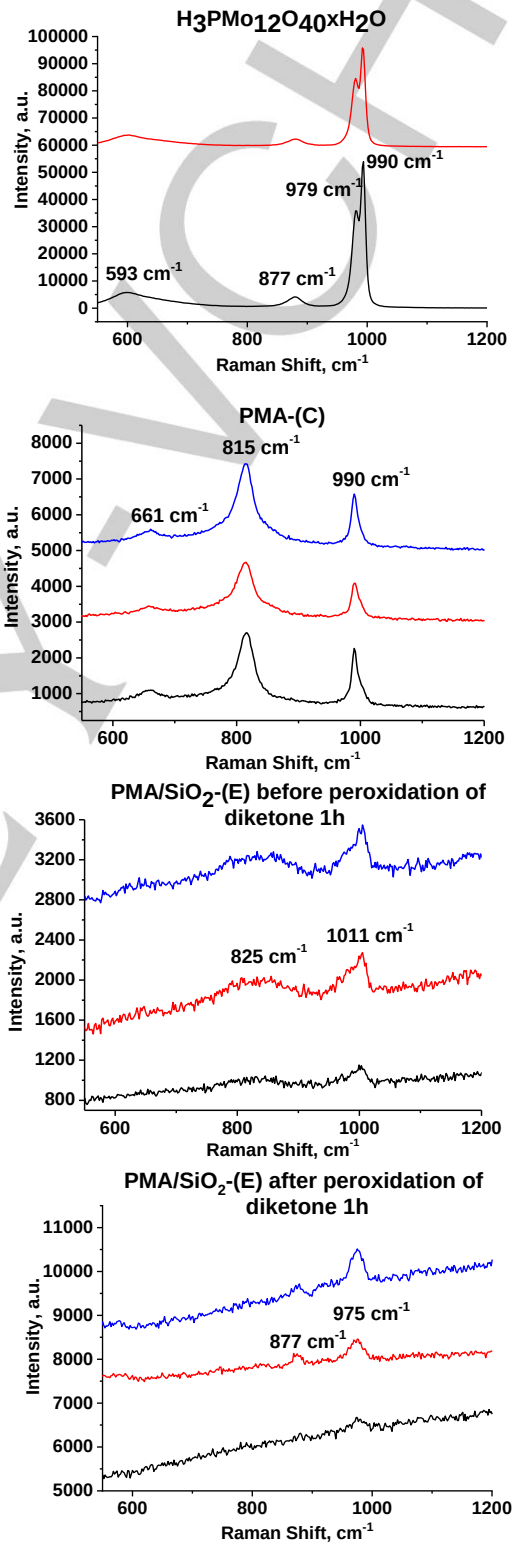


Figure 2. Raman spectra of $H_3PMo_{12}O_{40}\times H_2O$, PMA-**(C)**, PMA/$SiO_2$-**(E)** before and after the peroxidation of diketone **1h**

The high frequency shift of the first band compared to the similar band for bulk PMA with maxima at 990 cm^{-1} is typical for high loaded silica-supported 12-molybdophosphoric acid.[36] Thus, it can be assumed that in the process of preparation of PMA/SiO_2-**(E)**, the Keggin structure of PMA is partially destroyed. However, this does not have a significant negative effect on catalytic activity in the synthesis of ozonides with a high isolated yield of 90%. On the other hand, the broad Raman band with a maximum at 825cm^{-1} disappeared in the spectrum of PMA/SiO_2-**(E)** after peroxidation reaction of 1,5-diketone **1h**. Probably the water formed during this reaction promots regeneration of the Keggin structure of PMA after its partial destruction, as previously reported.[37]

Successful immobilization of PMA on the SiO_2 was confirmed by FT-IR analyses as shown in SI. Initial silica gel before any treatment exhibits such main IR bands as: bands at 801 and 468 cm^{-1} (symmetric stretching and bending modes of bulk Si–O–Si bond.), the band at 970 cm^{-1} (Si–OH stretching vibration of the surface silanol groups), the band at 1097 cm^{-1} (asymmetric stretching vibration of the structural siloxane bond Si–O–Si). The band at ca. 1637 cm^{-1} was due to the bending vibration of trapped water molecules. The broad band around 3442–3456 cm^{-1} is due to the vibration of HO–H of water molecules adsorbed on the silica surface and the stretching vibration of SiO–H bond. [26b, 27a, 30b] The FT-IR spectra of bulk $H_3PMo_{12}O_{40}\times H_2O$ shows bands at 1065, 962, 871, and 784 cm^{-1} which assigned to stretching vibrations ν_{as}(P-O_d), ν_{as}(Mo-O_t), ν_{as}(Mo-O_b-Mo) and ν_{as}(Mo-O_c-Mo), respectively. These bands are fully corresponding to the Keggin structure of $H_3PMo_{12}O_{40}\times H_2O$.[30a, 30c, 38] In the FT-IR spectrum of PMA/SiO_2-**(E)** the characteristic IR bands for $H_3PMo_{12}O_{40}\times H_2O$ is partly overlapped by SiO_2. The bands at 1065, 871, and 784 cm^{-1}, assigned to ν_{as}(P-O_d), ν_{as}(Mo-O_b-Mo) and ν_{as}(Mo-O_c-Mo), respectively is completely masked into the bands of the silica. However, the band at 962 cm^{-1} (ν_{as}(Mo-O_t)) corresponding to the Keggin structure of $H_3PMo_{12}O_{40}\times H_2O$ is clearly identified. Based on obtained results, we can conclude that $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$ supported on silica gel is mainly in the form of the Keggin structure and contains the fragment Mo=O.

We assume, that the difference in activity of PMA/SiO_2-**(D)** and PMA/SiO_2-**(E)** also depends on their different degree of hydration, which affects the mobility of the protons of PMA. The protons of can protonate diketone **1h** to facilitate the transfer of the peroxo group from the molybdenum peroxy complex to the carbonyl group. Thus we guess, that treatment of PMA/SiO_2-**(E)** with covered glass lid are optimal condition to provide the acid-catalyzed pathway of transformation of diketone **1h.**

From the wide angle XRD patterns of the supported sample PMA/SiO_2-**(E)**, no peak for PMA crystalline phases was found, and only the broad characteristic peak centered around 2θ = 22◦ attributed to amorphous silica appeared. Perhaps PMA is highly dispersed on SiO_2 due to the high surface area of these support material. This phenomenon was also observed by impregnating heteropoly acid $H_3PW_{12}O_{40}$ onto MCM-41[39] and PMA on mesoporous silica.[40] No crystal diffraction peaks of MoO_3 phase in PMA/SiO_2-**(E)** sample were found in XRD patterns despite the fact that it is reflected in the Raman spectra by the band at 825 cm^{-1}. This may be due to the low content of formed MoO_3 in PMA/SiO_2-**(E)** sample and due to finely dispersed, small particulate molybdenum oxide structure. According to XRD literature data[41] the most intense diffraction patterns from crystalline molybdenum oxide become noticeable when the Mo loading level of MoO_3 on SiO_2 is increased to 20 wt %.

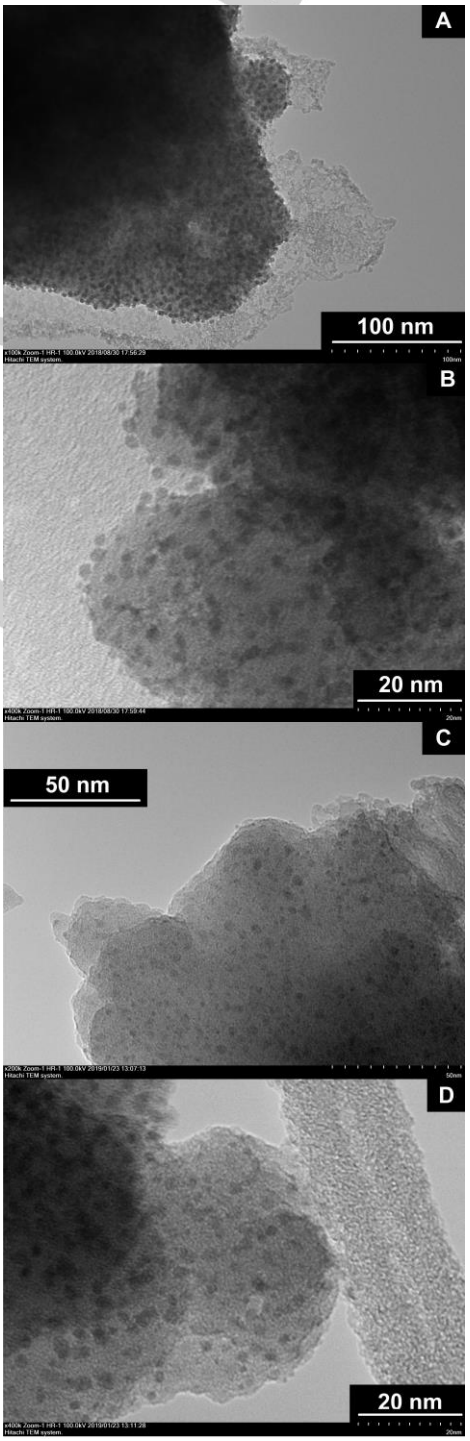


Figure 3. Characterization of PMA/SiO_2-**(E)** by TEM image A, B (before reaction), C, D (after reaction).

In addition, TEM characterization of $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$ supported on SiO_2 (PMA/SiO_2-**(E)**) was carried out. The TEM image of PMA/SiO_2-**(E)** is shown in Fig.3.

The TEM data shows that $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$ are nanoparticles on the SiO_2 support. The dark particles are $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$. The average particle size is around 2.6 nm for a fresh catalyst and around 2.1 nm for the catalyst after reaction (Fig. 4).

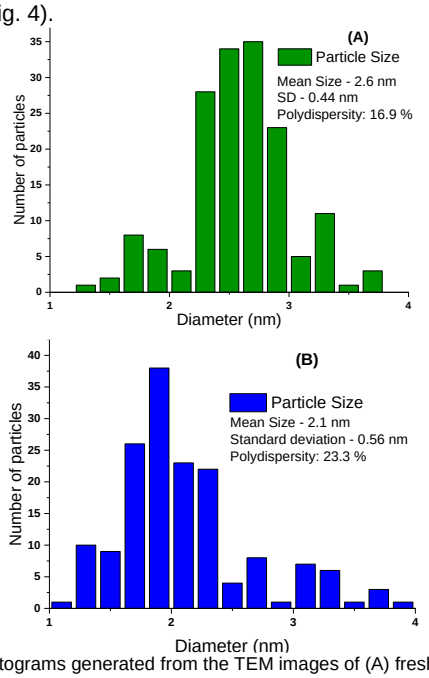


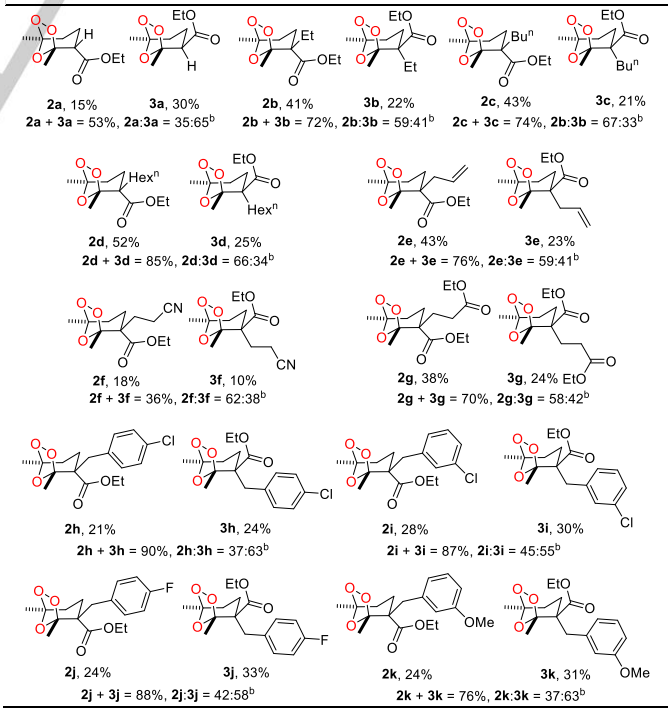
Figure 4. Histograms generated from the TEM images of (A) fresh and (B) used PMA/SiO_2-**(E)** catalyst.

The effect of amount of PMA/SiO_2-**(E)**, amount of H_2O_2, type of solvent, and the time of the reaction of peroxidation of diketone **1h** on the yield of ozonides **2h** and **3h** was investigated. At molar ratio of PMA : **1h** = 0.03 and 0.01, the yield of ozonides **2h** and **3h** was 65% and 8%, respectively (Runs 7 and 8, Table 1), at molar ratio of PMA : **1h** = 0.10 and 0.15, the yield of ozonides increased to 95 % on the isolated product (Runs 9 and 10, Table 1). Growth in the amount of PMA/SiO_2-**(E)** by a factor of 2 to 3 slightly increased the yield of ozonides from 90% to 95%. Thus, the optimal molar ratio of PMA : **1h** is 0.05 : 1.0. When using an equimolar amount of H_2O_2 towards to diketone **1h**, the yield of ozonides was 61% (Run 11, Table 1), with a 3-fold molar excess of H_2O_2, the yield of ozonides was 79% (Run 12, Table 1). The optimal molar ratio H_2O_2 : **1h** is 1.5: 1.0. Reducing the time of peroxidation of diketone **1h** to 0.5 hours led to a decrease in the yield of ozonides to 77% (Run 13, Table 1), while peroxidation of diketone **1h** for 24 hours afforded ozonides **2h** and **3h** in 93% yield (Run 14, Table 1). Thus, the optimal time for the reaction of peroxidation of diketone **1h** catalyzed by PMA/SiO_2-**(E)** is 1 hour and the molar ratio H_2O_2: PMA: diketone is 1.5: 0.05: 1.0. Toluene turned out to be the best solvent (the yield of ozonides was 90%); in benzene, CCl_4, CH_2Cl_2 or Et_2O the yield of ozonides decreases and does not exceed 82% (Runs 15-18, Table 1). With an increase in the weight content of PMA on SiO_2 to 30 wt.% (in the case of a weight content of PMA on SiO_2 > 30 wt.%, PMA is washed off from the surface of SiO_2) and at a molar ratio of PMA: diketone **1h** = 0.05: 1.0, a decrease in the yield of ozonides **2h** and **3h** is observed. In the case of PMA/SiO_2-**(F)**, the yield of ozonides **2h** and **3h** was 80%, and in the case of PMA/SiO_2-**(G)** it was 85% (Runs 19, 21, Table 1). At molar ratio of PMA: diketone **1h** = 0.1: 1.0, both in the case of PMA/SiO_2-**(F)** and in the case of PMA/SiO_2-**(G)**, the yield of ozonides was 95%. However, an increase in the yield on 5% compared with experiment 6 in table 1 requires an increase of the amount of PMA in 2 times. An increase in the amount of PMA/SiO_2-**(G)** to molar ratio of PMA : diketone **1h** = 0.15: 1.0 did not lead to an increase of the yield of ozonides. Thus, the optimal condition for the synthesis of ozonides from diketone **1h** and H_2O_2 was proposed for experiment 6 in table 1.

Under the conditions of Run 6 in Table 1, we decided to test our catalyst in the reaction of peroxidation of diketone **1h** on the gram scale. In this case, the yield of the target ozonides **2h** and **3h** was 57%. To our astonishment, it turned out that under the conditions of experiment No. 23 (Table 1), the peroxidation of 1 gram of diketone **1h** leads to the formation of ozonides with yield of 92%. Additionally, catalyst PMA/SiO_2-**(G)** can be recycled up to 3 times with some loss in the yield of ozonides **2h** and **3h** (92%, 84%, and 78% respectively). When using 4 times reused catalyst, the yield of ozonides decreased to 59%. This is probably due to the catalyst poisoning by initial diketone **1h**. The procedure for regeneration of PMA/SiO_2-**(G)** is in SI.

Under the optimal conditions (Run 6, Table 1), series of ozonides **2a-k** and **3a-k** were synthesized, containing various functional groups and fragments: alkene **2e**, **3e**, nitrile **2f**, **3f**, ester **2g**, **3g,** and aromatic core **2h- k**, **3h-k** (Table 2).

Table 2. Structures and isolated yields of the isomers and mixtures of isomeric ozonides **2a-k** and **3a-k** synthesized from 1,5-diketones **1a-k**.[a]

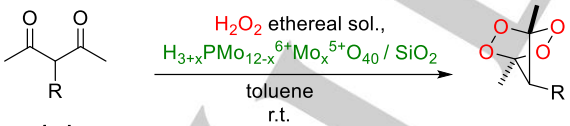


[a] A 7.4 M ethereal solution of H_2O_2 (0.186-0.300 mL, 1.38-2.23 mmol, 1.5 mole of H_2O_2 per mole of **1a-k**) and PMA/SiO_2-**(E)** (0.840 – 1.370 g; 10 wt.% of PMA; 0.046 - 0.075 mmol PMA, 0.15 mol of PMA / 1.0 mol 1,5- diketone **1a-k**) were successively added to a stirred solution of 1,5-diketone **1a-k** (0.300 g; 0.92-1.49 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1h. All reactions on the synthesis of ozonides were carried out in triplicate. In all replications the yields of ozonides were practically the same.

[b] The ratio of stereoisomers of ozonides **2a-k** : **3a-k** was determined by the ^{1}H NMR spectroscopic data.

Thus, we succeeded to develop the catalyst $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$ supported on SiO_2, which allows to synthesize ozonides with a yield up to 90% based on the isolated product under heterogeneous conditions from 1,5-diketones and hydrogen peroxide. The fact of the preparation of ozonides **2e**, **3e** with allyl substituent was amazing because double bond in diketone **1e** was not oxidized. It is well known that PMA / H_2O_2 system is able to oxidize and epoxidize unsaturated compounds.[25a, 25e, 25i] Peroxidation of diketone **1f** bearing CN group leads to the formation of ozonides with a moderate yield. All stereoisomeric ozonides **2a-k** and **3a-k** (Table 2) were separated and isolated in individual form by column chromatography and characterized by physicochemical methods of analysis. Synthesized novel ozonides **2h**, **3h**, **3j**, **3k**, are crystalline and melt without decomposition. Under the developed heterogeneous conditions, ozonides **3** are formed in higher yields compared to the case of homogeneous reactions.[16a,b]. This improvement is important for the search for biologically active compounds based on cyclic peroxides and the study of relationship between peroxide stereochemistry and activity.

Inspired by the results, we decided to enter $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$ supported on SiO_2 in peroxidation of 1,3-diketones **4a-k**. Taking into account that 1,3-diketones exist mainly in an enol form, the most expected result in heterogeneous conditions is the formation of hydroxy derivatives of diketones or more deep oxidation products. However, fortune turned out to be on our side, reaction of 1,3-diketones **4a-k** and hydrogen peroxide under the action of $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$ supported on SiO_2 selectively and with high yield gives bridged tetraoxanes **5a-k** (Scheme 2).



4a-k

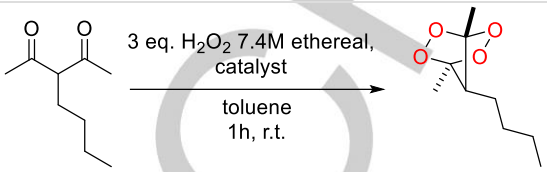
a: R = Me;
b: R = Et;
c: R = Allyl;
d: R = Bu;
e: R = Am;
f: R = *i*-Am;
g: R = Hex;
h: R = Oct;
i: R = $CH_2CH_2C(O)OEt$;
j: R = Ad;
k: R = 4-$BrC_6H_4CH_2$;

5a-k

Scheme 2. Synthesis of tetraoxanes **5a-k** from 1,3-diketones **4a-k**.

Peroxidation of 3-butylpentane-2,4-dione **4d** permitted to disclose the effect of the amount of $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$ supported on SiO_2 and the molar ratio of PMA:SiO_2 on the yield of tetraoxane **5d** (Table 3). The reaction of 3-butylpentane-2,4-dione **4d** with H_2O_2 was carried out at 20-25°C. The source of H_2O_2 was a 7.4M solution of H_2O_2 in Et_2O. Toluene was chosen as the solvent and the reaction time was 1 hour.

Table 3. Synthesis of 7-butyl-1,4-dimethyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane **5d** from 3-butylpentane-2,4-dione **4d** and H_2O_2[a]



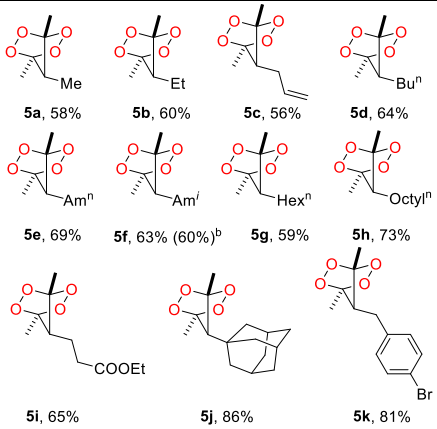
4d **5d**

Entry	Catalyst	Weight % PMA in PMA/SiO_2	Molar ratio PMA / **4d**	Yield of **5d** by NMR, % (isolated yield, %)
1	PMA/SiO_2-**(E)**	10	0.05	65
2	PMA/SiO_2-**(F)**	20	0.05	63
3	PMA/SiO_2-**(G)**	30	0.05	55
4	PMA/SiO_2-**(E)**	10	0.10	67
5	PMA/SiO_2-**(E)**	10	0.15	71
6	PMA/SiO_2-**(G)**	30	0.10	75 (64%)

[a] A 7.4 M ethereal solution of H_2O_2 (0.864 mL, 3.0 mol. of H_2O_2 / 1.0 mol. of 1,3-diketone **4d**) and PMA/SiO_2-**(E-G)** (0.05-0.15 mol. PMA / 1.0 mol. 1,3-diketone **4d**) were successively added to a stirred solution of 1,3-diketone **4d** (0.300 g; 1.92 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1h.

According to the optimization results, the best yield was achieved in Run 6. The isolated yield of tetraoxane **5d** was 64%. Taking into account the results of optimization and reaction conditions developed for tetraoxane **5d**, peroxides **5a-k** were synthesized from diketones **4a-k**, which contain alkyl substituents of various hydrocarbon chain lengths in the α-position, double bond and ester group (Table 4). In the case of the synthesis of tetraoxanes **5a-c**, safety precautions should be observed due to their explosive nature.

Table 4. Structures and isolated yields of tetraoxanes **5a-k** synthesized from the 1,3-diketones **4a-k**.[a]



5a, 58% **5b**, 60% **5c**, 56% **5d**, 64%
5e, 69% **5f**, 63% (60%)[b] **5g**, 59% **5h**, 73%
5i, 65% **5j**, 86% **5k**, 81%

[a] A 7.4 M ethereal solution of H_2O_2 (0.454 – 1.066 mL, 3.36 – 7.89 mmol.; 3 mol. of H_2O_2 per 1 mol. of **4a-k**) and PMA/SiO_2-**(G)** (0.682 – 1.600 g; 30 wt.% $H_3PMo_{12}O_{40}$; 0.112 - 0.263 mmol. $H_3PMo_{12}O_{40}$; 0.10 mol. $H_3PMo_{12}O_{40}$ / 1 mol. **4a-k**) were successively added to a stirred solution of 1,3-diketone **4a-k** (0.300 g; 1.12 – 2.63 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1h. All reactions on the synthesis of tetraoxanes were carried out in triplicate. In all replications the yields of tetraoxanes were practically the same.

[b] Reaction scale: 1.0 gram of 1,3-diketone **4f**.

Surprisingly, under heterogeneous conditions, tetraoxanes were formed in high yield. Expected hydro-, hydroxyperoxides or diketone oxidation products were not registered. Tetraoxanes **5j** and **5k** were obtained with yield above 80% based on the isolated product. From diketone **4c**, tetraoxane **5c** was formed with a good yield, despite the presence of alkenyl substituent. Tetraoxanes **5e**, **5f**, **5h**, and **5k** were previously unknown. Under the conditions of Run 6 (Table 3), tetraoxane **5f** was synthesized on a scale of 1.0 gram per starting diketone **4f**. The target tetraoxane **5f** was obtained in 60% yield based on the isolated product.

The developed catalyst $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$ supported on SiO_2 allows to synthesize bridged 1,2,4,5-tetraoxanes and bridged ozonides from 1,3- and 1,5-diketones with a high yield based on isolated product. It was surprising that the system $H_2O_2/H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}/SiO_2$ facilitates the assembly of cyclic peroxides, but not the formation of diketone oxidation products.

In vitro fungicidal activity of the synthesized ozonides and tetraoxanes.

In the next part of our study, it was discovered that the synthesized cyclic peroxides are a new class of fungicides. Prediction of the presence of fungicidal activity of tetraoxanes and ozonides was not possible because there are no fungicides containing peroxide fragment among existing commercial fungicides. Despite the fact that more than 200 fungicides with various (about 10) mechanisms of action are known,[42] there is an urgent need to create new classes of fungicides with a new mechanism of action. This is primarily due to the emergence of fungi resistance to fungicides and over time the fungicides used in agriculture become less effective.[43] Carbamates, azoles, amides, strobilurins, and anilines are the main classes of fungicides. According to our information, prior to this work, there were no data about the testing of peroxides against plant pathogen fungi.

The peroxides were tested against plant pathogenic fungi of various taxonomic classes, which cause great damage to agriculture and crop production: – *Venturia inaequalis* (*V.i.)* (causes the Apple scab disease)*; Rhizoctonia solani (R.s.)* (causes black scurf of potatoes), *Fusarium oxysporum (F.o.)* (causes rotting of the roots and wilting of lucerne, pea, soybean, wheat, cucumber, affects the vascular system of tomatoes), *Fusarium moniliforme* (*F.m.)* (causes fusarium of corn cob), *Bipolaris sorokiniana (B.s.)* (root rot of wheat, barley, rye, oats), *Sclerotinia sclerotiorum* (*S.s.)* (the causal agent of white rot of sunflower), *Fusarium graminearum (F.g.)* (the causal agent of fusarium rice, wheat and barley ears), *Fusarium heterosporum (F.h.)* (causes root rot and tracheomycosis of soybean), *Fusarium culmorum (F.c.)* (the causal agent of fusarium ear of wheat)), *Fusarium gibbosum (F.gb.)* (causes root rot and tracheomycosis of pea), *Fusarium nivale (Microdochium nivale)* (*F.m.n.*) (causes fusarium snow mold of cereals, affects winter wheat, rye), *Fusarium sporotrichiella* (*F.s.)* (causes fusarium of wheat, rye, barley), *Alternaria alternata (A.)* (causes black ear of wheat), *Pythium graminicola (P.sp.)* (affect cotton, wheat, turmeric, barley, rice, beans, peas, and sugarcane), *Phoma eupyrena (P.e.)* (causal agent of dark brown spot wheat, barley).

The effect of the tested peroxides on the mycelium radial growth in the potato-saccharose agar was measured in concentration 30 mg/L. Triadimefon and Kresoxim-methyl were used as reference compounds (Table 5).

Table 5. Growth inhibition of the mycelium of the pathogenic fungi by ozonides **2a-f**, **3a**, **3c-e**, and tetraoxanes **5a-j**.

№	Cmpd	Mycelium growth inhibition (I) ±(SD), % (C = 30 mg /L)													
		V. i.	***R. s.***	***F. o.***	***F. m.***	***B. s.***	***S. s.***	***F. g.***	***F. h.***	***F. c.***	***F. gb.***	***F. m.n.***	***F. s.***	***A.***	***P. sp.***	***P. e.***
1	**2a**	31±3	26±2	2±2	25±3	17±2	18±2	27±3	33±2	21±2	13±2	11±3	26±3	13±3	9±2	63±4
2	**3a**	10±2	38±3	2±2	10±2	25±3	14±1	19±2	29±2	26±3	5±2	18±4	-11	8±2	21±3	57±4
3	**2b**	33±3	18±1	18±3	14±2	20±2	11±1	46±4	59±3	54±5	23±2	19±3	57±5	8±2	30±3	57±5
4	**2c**	50±2	14±2	20±2	31±3	17±2	16±2	33±3	48±4	57±4	30±3	21±3	60±3	16±3	43±4	59±4
5	**3c**	38±2	46±2	13±1	22±2	25±3	17±2	32±2	26±2	31±3	17±2	21±2	40±2	31±4	36±3	40±3
6	**2d**	3±2	49±3	19±4	45±5	31±5	8±4	17±2	30±4	14±6	19±3	2±1	40±4	20±2	5±4	24±2
7	**3d**	42±8	53±5	30±4	46±3	21±4	10±3	32±2	12±3	23±3	24±2	23±5	49±4	28±2	15±5	28±2
8	**2e**	31±3	85±3	53±4	24±3	31±2	31±2	64±1	61±2	19±4	37±2	39±4	47±4	21±2	44±3	28±2
9	**3e**	45±4	91±2	76±5	50±4	47±3	42±3	94±1	75±6	40±4	67±3	40±4	58±3	32±2	37±5	40±3
10	**2f**	31±2	12±2	26±4	7±2	18±2	17±3	34±1	49±3	8±3	24±2	18±3	31±4	12±1	47±3	40±1
11	**5a**	88±5	**100**	99±1	**100**	66±3	96±1	90±1	**100**	**100**	88±2	84±2	97±2	56±3	98±1	86±5
12	**5b**	88±4	**100**	97±1	**100**	68±3	69±3	88±1	**100**	99±1	95±2	82±2	**100**	58±3	94	78±6
13	**5c**	37±7	**100**	**100**	**100**	**100**	52±3	97±1	**100**	99±1	**100**	**100**	**100**	47±7	**100**	90±4
14	**5d**	88±8	**100**	95±1	**100**	71±3	71±2	90±1	97±2	99±1	90±1	83±3	95±2	58±6	99±1	76±5
15	**5e**	**100**	**100**	**100**	**100**	68±2	48±3	**100**	**100**	**100**	**100**	**100**	**100**	49±3	98±1	71±1

16	**5f**	**100**	**100**	97±1	97±1	68±3	31±1	97±2	96±1	**100**	**100**	96±1	99±1	32±2	97±1	77±4
17	**5g**	90±1	**100**	**100**	**100**	52±2	38±4	97±1	**100**	**100**	97±1	97±1	100	52±2	**100**	70±3
18	**5h**	74±6	98±2	71±6	96±2	71±3	42±1	91±6	**100**	85±5	**100**	89±5	94±5	56±4	93±1	**100**
19	**5i**	15±5	67±3	39±3	50±3	9±4	25±2	19±1	8±3	-2±1	12±3	10±2	22±5	9±2	52±3	5±2
20	**5j**	54±5	98±1	53±4	80±2	81±2	42±3	99±1	93±2	**100**	97±1	71±2	77±2	53±2	75±4	73±2
21	**5k**	26±6	**100**	30±2	98±2	64±2	20±1	**100**	98±2	68±3	99±2	59±4	74±3	29±2	59±4	37±2
22	**Triadimefon**	78±1	62±2	83±2	89±1	68±2	55±2	49±7	79±5	77±2	34±3	54±2	80±3	39±1	36±1	26±4
23	**Krezoxim-methyl**	89±1	**100**	69±1	60±2	54±2	47±1	59±6	76±6	43±6	66±6	68±2	56±6	65±2	**100**	**100**

SD : standard deviation

Among the investigated ozonides **2a-f**, **3a**, **3c-e**, the best fungicidal activity was shown by ozonide **3e**, which contains an allylic substituent. It was the most active against 11 of 15 fungi, except *V.i.*, *F.c.*, *F.s.*, and *P.e*. When using ozonide **3e** at a concentration of 30 mg / L, an inhibition of mycelium growth of more than 50% was observed in 7 of 15 fungi, namely against *R.s.*, *F.o.*, *F.m.*, *F.g.*, *F.h.*, *F.g.*, and *F.s.* Ozonide **3e** is superior to the commercially used fungicide Triadimefon against such fungi as *R.s.*, *F.g.*, *F.gb.*, *P.sp*, and *P.e*, and against *F.o*, *F.g.*, *F.gb.*, and *F.s.* – is superior to Kresoxim-methyl. Against *F.h*. ozonide **3e** is comparable in activity to Kresoxim-methyl. Ozonide **2c** was the most effective among ozonides against *V.i.*, *F.c.* and *F.s*; against *F.c.*, *F.s.* it was more active than Kresoxim-methyl. All tested ozonides, with the exception of ozonide **2d** versus *P.e.* turned out to be more active than Triadimefon, the most active among them was ozonide **2a**, mycelium growth inhibition of *P.e.* up to 63%. Against *P.sp.* the most active ozonide was ozonide **2f**, which turned out to be more active than Triadimefon, mycelium growth inhibition of *P.sp.* was 47% vs. 36% respectively. Ozonide **2e** was more active than Triadimefon against *R.s.*, *F.gb.*, *P.sp.*, and *P.e*. Towards to *F.g.* ozonide **2e** is more active than Triadimefon and Kresoxim-methyl.

Very interesting and unprecedented results were obtained in the study of tetraoxanes **5a-k**. All tested tetraoxanes containing alkyl substituents showed a very high fungicidal activity at concentration of 30 mg / L. All tetraoxanes, with the exception of **5i**, exhibit 100% inhibition of the growth of the mycelium (*I* = 100 %) in a wide range of phytopathogenic fungi and are superior in activity to the commercial fungicides Triadimefon and Kresoxim-methyl. However, only in the case of *Alternaria alternata (A.)*, the inhibition of mycelium growth did not exceed 58%. The most active among tetraoxanes **5a-k** was tetraoxane **5e**, which contains amyl substituent. Tetraoxane **5e** completely suppresses the growth of mycelium in 10 out of 15 fungi with the exception of *B.s.*, *S.s.*, *A.*, *P.sp.*, *P.e*. and is superior in activity to both Triadimefon and Kresoxim-methyl. Against *S.s.* tetraoxane **5a** is the most active (*I* = 96%); vs. A., tetraoxanes **5b** and **5d** (*I* = 58%); vs. *P.sp.* - tetraoxanes **5c** and **5g** (*I* = 100%); vs. *P.e.* - tetraoxane **5h** (*I* = 100%). It is worth noting that the presence of a substituent with ester functional group or bulky benzyl substituent in the tetraoxane molecule leads to a sharp decrease in the fungicidal activity, the length of alkyl substituent from C1 to C8 has little effect on the fungicidal activity.

Further, for the most active tetraoxanes **5a**, **5c**, **5e-g**, we determined EC_{50} against key phytopathogens, such as *Venturia inaequalis* (*V.i.), Rhizoctonia solani (R.s.)*, *Fusarium oxysporum (F.o.)*, *Fusarium moniliforme* (*F.m.)*, *Bipolaris sorokiniana (B.s.)*, *Sclerotinia sclerotiorum* (*S.s.)* (Table 6).

Table 6. Fungicidal activity (EC_{50}) of tetraoxanes **5a**, **5c**, **5e-g**.

№	Cmpd	EC_{50} (mg /L)±SD					
		V. i.	***R. s.***	***F. o.***	***F. m.***	***B. s.***	***S. s.***
1	**5a**	14.2±1.6	5.5±1.2	12.8±2.1	12.3±2.1	5.0±1.0	13.6±0.8
2	**5c**	>30.0	6.5±0.8	12.4±2.5	12.1±2.2	12.7±3.1	28.2±1.4
3	**5e**	8.9±1.4	3.4±0.9	10.2±1.7	10.5±1.6	2.8±0.4	>30
4	**5f**	12.5±1.2	4.8±0.5	12.8±1.1	13.4±0.9	15.0±3.5	>30
5	**5g**	15.6±0.9	4.4±0.5	12.3±2.6	7.8±0.6	27.8±2.5	>30
6	**Triadime-fon**	7.6±0.4	23.2±3.2	2.6±0.2	2.1±0.2	8.7±0.7	18.3±2.2
7	**Krezoxim-methyl**	2.2±0.1	<0.3	<0.3	7.6±1.3	18.2±1.6	>30.0

SD : standard deviation

The results in Table 6 show that tetraoxanes **5a**, **5c**, **5e-g** are more potent fungicides than Triadimefon against *R.s.*, but inferior to Kresoxim-methyl. Tetraoxanes **5a**, **5c**, and **5f** are more effective than Kresoxim-methyl vs. *B.s*, and tetraoxane **5e** is more effective than Triadimefon, and Kresoxim-methyl vs. *B.s*. Tetraoxane 5a shows higher fungicidal properties than Triadimefon and Kresoxim-methyl vs. *S.s.*

The results obtained in this work demonstrate that cyclic peroxides can be considered as a new class of fungicides and they are of great interest for further research in order to develop the next generation of plant protection agents.

Conclusions

The catalyst $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}$ supported on SiO_2 was discovered, which under heterogeneous conditions allows to carry out peroxidation of 1,3- and 1,5-diketones. Non-polar solvents such as toluene, benzene, diethyl ether, dichloromethane or carbon tetrachloride were proposed as the solvents, since the catalyst does not dissolve in them. The development of methods for the synthesis of peroxides under heterogeneous conditions is an important and at the same time complex methodological task for industry and valuable contribution to the chemistry of peroxides. When using $H_{3+x}PMo_{12-x}{}^{+6}Mo_x{}^{+5}O_{40}/SiO_2$, only target cyclic peroxides are formed. A new class of fungicides for plant protection has been discovered - cyclic peroxides. None of the agrochemical fungicides contains a peroxide moiety. The bridged ozonides

and bridged tetraoxanes possess fungicidal activity that exceeds the activity of such widely used fungicides as Triadimefon and Kresoxim-methyl.

Experimental Section

Caution: Although we have encountered no difficulties in working with the peroxides described below, the proper precautions, such as the use of shields, fume hoods and the avoidance of transition metal salts, heating and shaking, should be taken. In the case of the synthesis of tetraoxanes 5a-c, safety precautions should be observed due to their explosive nature. When working with a 7.4 M solution of H_2O_2 in diethyl ether, use gloves and work in a fume hood. 7.4 M ethereal solution of H_2O_2 should be stored below 5°C.

NMR spectra were recorded on a commercial instrument (300.13 MHz for ^{1}H, 75.48 MHz for ^{13}C) in $CDCl_3$. High resolution mass spectra (HRMS) were measured using electrospray ionization (ESI).[108] The measurements were done in a positive ion mode (interface capillary voltage 4500 V); the mass ratio was from m/z 50 to 3000 Da; external/internal calibration was done with Electrospray Calibrant Solution. A syringe injection was used for solutions in MeCN (flow rate 3 □L/min). Nitrogen was applied as a dry gas; interface temperature was set at 180 □C. IR spectra were recorded on FT-IR spectrometer. All the Raman spectra were measured using InVia Reflex Raman microscope (Renishaw, UK) in confocal mode with 633 nm HeNe laser (17 mW). A neutral density filter with an optical throughput of 100% was used. Instrument adjustment was made applying silicon monocrystalline wafer. The focus length was 250 mm, size of the laser spot was 5 um with diffraction monochromator 1200 groves/mm. All spectra were recorded applying 50x objective and 3s acquisition time (except for MoO_3 it was 1 s) with 3 accumulations. The Raman spectra in each figure corresponds to different points on a surface of the described sample. TGA was performed on the "Derivatograth-C" (MOM, Hungary) in air at a heating rate of 10 °C/min on a sample of about 25 mg by weight. Target-oriented approach was utilized for the optimization of the analytic measurements.[44] Before measurements the samples were mounted on a 3 mm copper grid with lacey carbon film and fixed in a grid holder. Samples morphology was studied using Hitachi transmission electron microscope (TEM). Images were acquired in bright-field TEM mode at 100 kV accelerating voltage. The TLC analysis was carried out on silica gel chromatography plates Macherey-Nagel Alugram UV254; Sorbent: Silica 60, specific surface (BET) ~ 500 m^2/g, mean pore size 60 Å, specific pore volume 0.75 mL/g, particle size 5–17 μm; Binder: highly polymeric product, which is stable in almost all organic solvents and resistant towards aggressive visualization reagents. The melting points were determined on a Kofler hot-stage apparatus. Chromatography of 1,5-diketones was performed on silica gel (0.060-0.200 mm, 60 A, CAS 7631-86-9). Chromatography of ozonides was performed on silica gel (0.040-0.060 mm, 60 A, CAS 7631-86-9). Dichloromethane, toluene, petroleum ether (PE) (40/70), ethyl acetate (EA), ethyl acetoacetate, methyl vinyl ketone, benzyl and alkyl halides, H_2O_2 (35% aqueous solution), $MgSO_4$, $NaHCO_3$, NaI, $CeCl_3$•$7H_2O$, $Na_2S_2O_3$ were purchased from Acros. A solution of H_2O_2 in Et_2O (7.4 M) was prepared by the extraction with Et_2O (5×100 mL) from a 35% aqueous solution (100 mL) followed by drying over $MgSO_4$ and removal of part of Et_2O under a water jet vacuum at 20-25 °C. Toluene was distilled over Na.

Procedures for preparation of promoters for peroxidation of 1,5-diketone 1h

a) Procedure for preparation PMA-(A)

$H_3PMo_{12}O_{40}$×H_2O (0.625 g of 80% phosphomolybdic acid; 0.500 g, 0.27 mmol of $H_3PMo_{12}O_{40}$) was placed in open Petri dish (diameter 9.5 cm; PMA was distributed evenly over the surface) and heated in an oven at 150 °C for 2 hours.

b) Procedure for preparation PMA-(B)

$H_3PMo_{12}O_{40}$×H_2O (0.625 g of 80% phosphomolybdic acid; 0.500 g, 0.27 mmol of $H_3PMo_{12}O_{40}$) was stepwise heated on a heating table of the magnetic stirrer in open Petri dish (diameter 9.5 cm, PMA was distributed evenly over the surface) with an increase of temperature from r.t. to 150 ° C: at 40 °C for 30 min., then at 60 °C - 30 min.; at 80 °C - 30 min.; at 100 °C - 30 min.; and then at 150 °C for one hour.

c) Procedure for preparation PMA-(C)

$H_3PMo_{12}O_{40}$×H_2O (0.625 g of 80% phosphomolybdic acid; 0.500 g, 0.27 mmol of $H_3PMo_{12}O_{40}$) was placed in a beaker and dissolved in ethanol (15 mL). The solvent was evaporated at 150 °C and 1 atm. in air atmosphere on a heating table of the magnetic stirrer, and the resulting residue was heated at 150 °C for 1 hour. The resulting residue was ground by grinding in a mortar.

d) Procedure for preparation PMA/SiO_2-(D)

A silica gel SiO_2 (4.5 g, 60 Å, 0.060-0.200 mm, S=470-530 m^2/g) was added to intensively stirred solution of $H_3PMo_{12}O_{40}$×H_2O (0.625 g of 80% phosphomolybdic acid; 0.500 g, 0.27 mmol of $H_3PMo_{12}O_{40}$) in ethanol (50 mL) at 20-25 °C. The suspension was stirred at 20-25 °C for 10 min. Then the solvent was evaporated under a water jet vacuum at 30 °C. After that, the resulting PMA/SiO_2 (10 wt.% $H_3PMo_{12}O_{40}$) was stepwise heated on a heating table of the magnetic stirrer in open Petri dish (diameter 9.5 cm, PMA/SiO_2 was distributed evenly over the surface, the height of the layer was not more than 3 mm) with an increase of temperature from r.t. to 150 ° C: at 40 °C for 30 min., then at 60 °C - 30 min.; at 80 °C - 30 min.; at 100 °C - 30 min.; and then at 150 °C for one hour.

e) Procedure for preparation PMA/SiO_2-(E)

Silica gel SiO_2 (4.5 g, 60 Å, 0.060-0.200 mm, S=470-530 m^2/g) was added to intensively stirred solution of $H_3PMo_{12}O_{40}$×H_2O (0.625 g of 80% phosphomolybdic acid; 0.500 g, 0.27 mmol of $H_3PMo_{12}O_{40}$) in ethanol (50 mL) at 20-25 °C. The suspension was stirred at 20-25 °C for 10 min. Then the solvent was evaporated under a water jet vacuum at 30 °C. After that, the resulting PMA/SiO_2 (10 wt.% $H_3PMo_{12}O_{40}$) was stepwise heated on a heating table of the magnetic stirrer in open Petri dish (diameter 9.5 cm, PMA/SiO_2 was distributed evenly over the surface, the height of the layer was not more than 3 mm) with an increase of temperature from r.t. to 150 ° C: at 40 °C for 30 min., then at 60 °C - 30 min.; at 80 °C - 30 min.; at 100 °C - 30 min.; and then at 150 °C for one hour (upon reaching 150 °C the Petri dish was immediately covered with Petri dish lid).

f) Procedure for preparation PMA/SiO_2-(F)

Silica gel SiO_2 (4.0 g, 60 Å, 0.060-0.200 mm, S=470-530 m^2/g) was added to intensively stirred solution of $H_3PMo_{12}O_{40}$×H_2O (1.250 g of 80% phosphomolybdic acid; 1.00 g, 0.54 mmol of $H_3PMo_{12}O_{40}$) in ethanol (50 mL) at 20-25 °C. The suspension was stirred at 20-25 °C for 10 min. Then the solvent was evaporated under a water jet vacuum at 30 °C. After that, the resulting PMA/SiO_2 (20 wt.% $H_3PMo_{12}O_{40}$) was stepwise heated on a heating table of the magnetic stirrer in open Petri dish

(diameter 9.5 cm, PMA/SiO_2 was distributed evenly over the surface, the height of the layer was not more than 3 mm) with an increase of temperature from r.t. to 150 ° C: at 40 °C for 30 min., then at 60 °C - 30 min.; at 80 °C - 30 min.; at 100 °C - 30 min.; and then at 150 °C for one hour (upon reaching 150 °C the Petri dish was immediately covered with Petri dish lid).

g) Procedure for preparation PMA/SiO_2-(G)

Silica gel SiO_2 (3.5 g, 60 Å, 0.060-0.200 mm, S=470-530 m^2/g) was added to intensively stirred solution of $H_3PMo_{12}O_{40}\times H_2O$ (1.875 g of 80% phosphomolybdic acid; 1.500 g, 0.81 mmol of $H_3PMo_{12}O_{40}$) in ethanol (50 mL) at 20-25 °C. The suspension was stirred at 20-25 °C for 10 min. Then the solvent was evaporated under a water jet vacuum at 30 °C. After that, the resulting PMA/SiO_2 (30 wt.% $H_3PMo_{12}O_{40}$) was stepwise heated on a heating table of the magnetic stirrer in open Petri dish (diameter 9.5 cm, PMA/SiO_2 was distributed evenly over the surface, the height of the layer was not more than 3 mm) with an increase of temperature from r.t. to 150 ° C: at 40 °C for 30 min., then at 60 °C - 30 min.; at 80 °C - 30 min.; at 100 °C - 30 min.; and then at 150 °C for one hour (upon reaching 150 °C the Petri dish was immediately covered with Petri dish lid).

h) Regeneration procedure of PMA/SiO_2-(G)

After reaction the filtered and washed with CH_2Cl_2 (3 × 10 ml) catalyst PMA/SiO_2^G was stepwise heated on a heating table of the magnetic stirrer in Petri Dish (diameter 9.5 cm) with an increase of temperature from r.t. to 150 ° C: at 40 °C for 30 min., then at 60 °C - 30 min.; at 80 °C - 30 min.; at 100 °C - 30 min.; and then at 150 °C for one hour (upon reaching 150 °C the Petri Dish was immediately covered with Petri Dish lid).

Synthesis of 1,5-diketones 1a-k and 1,3-diketones 4a-k.

1,5–Diketones **1a–k** were synthesized according to a known procedures.[16, 28d] 1,5–Diketones **1h-k** are previously undescribed compounds. Other 1,5-diketones are known compounds. 1,3-Diketones **4a-h,k**,[45] **4i**,[46] **4j**,[47] were synthesized according to the known procedures.

Typical procedure for preparation of 1,5–diketones 1h-k: Methyl vinyl ketone (1.2 mol / 1.0 mol of β-keto ester), cerium (III) chloride (0.2 mol / 1.0 mol of β-keto ester), and sodium iodide (0.1 mol / 1.0 mol of β-keto ester) were successively added with stirring to the corresponding β-keto ester (1.5 g. 5.89-6.29 mmol) at 20−25 °C. Solid β-keto esters were dissolved in 5 mL CH_3CN prior to the reaction whereas liquid β-keto esters can be used neat. The reaction mixture was stirred at room temperature for 24 h. Then EtOAc (30 mL) was added, and the reaction mixture was stirred another 30 min. After that the mixture was transferred into a separating funnel, and H_2O (10 mL) and two drops of 36% aq. HCl were added. The aqueous phase was separated; the organic phase was washed by saturated aq. sol. of $Na_2S_2O_3$ and then with water (2×10 mL). The organic phase was dried over $MgSO_4$ and filtered. The solvent was removed in the vacuum of a water jet pump. 1,5-Diketones were isolated by chromatography on SiO_2 using PE : EA mixture as the eluent with a gradient of EA from 10 to 90 vol. % Compounds: **1h**: 1.41 g, 4.35 mmol, yield 74%; **1i**: 1.66 g, 3.59 mmol, yield 61%; **1j**: 1.18 g, 3.84 mmol, yield 61%; **1k** 1.59 g, 4.97 mmol, yield 83%.

Ethyl 2-acetyl-2-(4-chlorobenzyl)-5-oxohexanoate, 1h

White crystals. Mp = 63-65 °C. Yield 74%, 1.58 g, 5.27 mmol. R_f = 0.57 (TLC, PE : EA, 2 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.25 (t, J = 7.3 Hz, 3H), 2.06-2.14 (m, 8H), 2.33-2.39 (m, 2H), 3.05 (d, J = 14.2 Hz, 1H), 3.18 (d, J = 14.2 Hz, 1H), 4.14-4.17 (m, 2H), 6.99 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.2 Hz, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.1, 25.6, 27.7, 30.1, 37.7, 38.3, 61.7, 63.9, 128.6, 131.3, 133.1, 134.5, 171.6, 205.1, 206.9; Anal. Calcd for $C_{17}H_{21}ClO_4$: C, 62.87; H, 6.52; Cl, 10.91. Found: C, 62.89; H, 6.53; Cl, 10.93. HRMS (ESI-TOF): m/z [M+Na]$^+$: calculated for $[C_{17}H_{21}ClNaO_4]^+$: 347.1021; found: 347.1013

Ethyl 2-acetyl-2-(3-chlorobenzyl)-5-oxohexanoate, 1i

White crystals. Mp = 56-58 °C. Yield 61%, 1.66 g, 3.59 mmol. R_f = 0.52 (TLC, PE : EA, 2 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.23 (t, J = 7.3 Hz, 3H), 2.04-2.12 (m, 8H), 2.32-2.42 (m, 2H), 3.04 (d, J = 14.2 Hz, 1H), 3.18 (d, J = 14.2 Hz, 1H), 4.12-4.20 (m, 2H), 6.92-7.18 (m, 4H). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.0, 25.6, 27.6, 30.1, 37.9, 38.2, 61.7, 63.8, 127.3, 128.1, 129.7, 130.0, 134.2, 138.1, 171.5, 204.9, 206.8; Anal. Calcd for $C_{17}H_{21}ClO_4$: C, 62.87; H, 6.52; Cl, 10.91. Found: C, 62.86; H, 6.51; Cl, 10.92. HRMS (ESI-TOF): m/z [M+Na]$^+$: calculated for $[C_{17}H_{21}ClNaO_4]^+$: 347.1021; found: 347.1018

Ethyl 2-acetyl-2-(4-fluorobenzyl)-5-oxohexanoate, 1j

White crystals. Mp = 56-58 °C. Yield 61%, 1.18 g, 3.84 mmol. R_f = 0.52 (TLC, PE : EA, 2 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.23 (t, J = 7.3 Hz, 3H), 2.07-2.11 (m, 8H), 2.33-2.42 (m, 2H), 3.04 (d, J = 14.2 Hz, 1H), 3.18 (d, J = 14.2 Hz, 1H), 4.12-4.20 (m, 2H), 6.90-7.04 (m, 4H). ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.0, 25.6, 27.7, 30.1, 37.6, 38.3, 61.6, 63.9, 115.4 (d, $^2J_{CF}$ = 21.3 Hz), 131.5 (d, $^3J_{CF}$ = 7.9 Hz), 131.7 (d, $^4J_{CH}$ = 3.4 Hz), 162.1 (d, $^1J_{CF}$ = 245.8 Hz), 171.2, 205.1, 206.9; Anal. Calcd for $C_{17}H_{21}FO_4$: C, 66.22; H, 6.86; F, 6.16. Found: C, 66.24; H, 6.87; F, 6.17. HRMS (ESI-TOF): m/z [M+Na]$^+$: calculated for $[C_{17}H_{21}FNaO_4]^+$: 331.1316; found: 331.1314.

Ethyl 2-acetyl-2-(3-methoxybenzyl)-5-oxohexanoate, 1k

White crystals. Mp = 39-40 °C. Yield 83%, 1.59 g, 4.97 mmol. R_f = 0.21 (TLC, PE : EA, 5 : 1); ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.25 (t, J = 7.3 Hz, 3H), 2.07-2.17 (m, 8H), 2.33-2.42 (m, 2H), 3.09 (d, J = 14.2 Hz, 1H), 3.17 (d, J = 14.2 Hz, 1H), 3.75 (s, 3H), 4.16 (q, J = 7.1 Hz, 2H), 6.60-6.76 (m, 3H), 7.15 (t, J = 7.1 Hz, 1H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.1, 25.6, 27.6, 30.1, 38.3, 38.4, 55.2, 61.6, 64.0, 112.4, 115.9, 122.3, 129.5, 137.5, 159.7, 171.8, 205.2, 207.0; Anal. Calcd for $C_{18}H_{24}O_5$: C, 67.48; H, 7.55. Found: C, 67.49; H, 7.56. HRMS (ESI-TOF): m/z [M+Na]$^+$: calculated for $[C_{18}H_{24}NaO_5]^+$: 343.1516; found: 343.1516.

Procedure for peroxidation of 1h with use of 7.4 M ethereal solution of H_2O_2 and PMA or PMA-(A-C) (Table 1, Runs 1-4)

A 7.4 M ethereal solution of H_2O_2 (0.186 mL, 1.38 mmol, 1.5 mol H_2O_2 / 1.0 mol of 1,5-diketone **1h**) and PMA (0.105g, 0.046 mmol of $H_3PMo_{12}O_{40}$) or PMA-**(A-C)** (0.084 g, 0.046 mmol of $H_3PMo_{12}O_{40}$) were successively added to a stirred solution of 1,5-diketone **1h** (0.300 g; 0.92 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump. Mixture of ozonides **2h** + **3h** was isolated by chromatography on SiO_2 using PE : EA mixture as the eluent with a gradient of EA from 5 to 20 vol. % The ratio of ozonides **2h**:**3h** was determined by the ^{1}H NMR spectroscopic data.

Procedure for peroxidation of 1h with use of 7.4 M ethereal solution of H_2O_2 and PMA/SiO_2-(D) or PMA/SiO_2-(E) (Table 1, Runs 5-18)

A 7.4 M ethereal solution of H_2O_2 (0.121 – 0.363 mL, 0.92 – 2.76 mmol, 1.0 – 3.0 mol H_2O_2 / 1.0 mol of 1,5-diketone **1h**) and PMA/SiO_2-**(D)** or PMA/SiO_2-**(E)** (0.165 – 2.518 g, 10 wt.% $H_3PMo_{12}O_{40}$, 0.009 – 0.138 mmol of $H_3PMo_{12}O_{40}$, 0.01-0.15 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,5- diketone **1h**) were successively added to a stirred solution of 1,5-diketone **1h** (0.300 g; 0.92 mmol) in toluene, CCl_4, CH_2Cl_2 or Et_2O (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 0.5-24 h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump. Mixture of ozonides **2h** + **3h** was isolated by chromatography on SiO_2 using PE : EA mixture as the eluent with a gradient of EA from 5 to 20 vol. % The ratio of ozonides **2h**:**3h** was determined by the ^{1}H NMR spectroscopic data.

Procedure for peroxidation of 1h with use of 7.4 M ethereal solution of H_2O_2 and PMA/SiO_2-(F) (Table 1, Runs 19-20)

A 7.4 M ethereal solution of H_2O_2 (0.186 mL, 1.38 mmol, 1.5 mol H_2O_2 / 1.0 mol of 1,5-diketone **1h**) and PMA/SiO_2-**(F)** (0.420 – 0.840 g, 20 wt.% $H_3PMo_{12}O_{40}$, 0.046 – 0.092 mmol of $H_3PMo_{12}O_{40}$, 0.05-0.10 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,5- diketone **1h**) were successively added to a stirred solution of 1,5-diketone **1h** (0.300 g; 0.92 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1 h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump. Mixture of ozonides **2h** + **3h** was isolated by chromatography on SiO_2 using PE : EA mixture as the eluent with a gradient of EA from 5 to 20 vol. % The ratio of ozonides **2h**:**3h** was determined by the ^{1}H NMR spectroscopic data.

Procedure for peroxidation of 1h with use of 7.4 M ethereal solution of H_2O_2 and PMA/SiO_2-(G) (Table 1, Runs 21-23)

A 7.4 M ethereal solution of H_2O_2 (0.186 mL, 1.38 mmol, 1.5 mol H_2O_2 / 1.0 mol of 1,5-diketone **1h**) and PMA/SiO_2-**(G)** (0.420 – 1.260 g, 30 wt.% $H_3PMo_{12}O_{40}$, 0.046 – 0.138 mmol of $H_3PMo_{12}O_{40}$, 0.05-0.15 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,5- diketone **1h**) were successively added to a stirred solution of 1,5-diketone **1h** (0.300 g; 0.92 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1 h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump. Mixture of ozonides **2h** + **3h** was isolated by chromatography on SiO_2 using PE : EA mixture as the eluent with a gradient of EA from 5 to 20 vol. % The ratio of ozonides **2h**:**3h** was determined by the ^{1}H NMR spectroscopic data.

General procedure for the synthesis of ozonides from diketones 1a-k

A 7.4 M ethereal solution of H_2O_2 (0.186-0.301 mL, 1.38-2.23 mmol, 1.5 mol H_2O_2 / 1.0 mol of 1,5-diketone **1a-k**) and PMA/SiO_2-**(E)** (0.840 – 1.370 g, 10 wt.% $H_3PMo_{12}O_{40}$, 0.046 - 0.075 mmol of $H_3PMo_{12}O_{40}$, 0.05 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,5- diketone **1a-k**) were successively added to a stirred solution of 1,5-diketone **1a-k** (0.300 g; 0.92-1.49 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 0.5-24 h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump.

Ozonides **2a-k**, and **3a-k** in individual form were isolated by chromatography on SiO_2 using PE : EA mixture as the eluent with a gradient of EA from 1 to 5 vol. % Compounds: **2a**: 74.5 mg, 0.34 mmol, yield 23%; **3a**: 58.3 mg, 0.27 mmol, yield 18%; **2b**: 112.4 mg, 0.46 mmol, yield 35%; **3b**: 67.4 mg, 0.27 mmol, yield 21%; **2c**: 121.1 mg, 0.44 mmol, yield 38%; **3c**: 76.5 mg, 0.28 mmol, yield 24% **2d**: 152.1 mg, 0.5 mmol, yield 48%; **3d**: 69.7 mg, 0.23 mmol, yield 24%; **2e**: 128 mg, 0.5 mmol, yield 40%; **3e**: 73.6 mg, 0.28 mmol, yield 23%; **2f**: 47.8 mg, 0.17 mmol, yield 15%; **3f**: 41.4 mg, 0.15 mmol, yield 13%; **2g**: 113.7 mg, 0.36 mmol, yield 36%; **3g**: 72.6 mg, 0.23 mmol, yield 23%; **2h**: 66.0 mg, 0.19 mmol, yield 21%; **3h**: 75.5 mg, 0.22 mmol, yield 24%; **2i**: 88.0 mg, 0.26 mmol, yield 28%; **3i**: 94.3 mg, 0.27 mmol, yield 30 %; **2j**: 75.7 mg, 0.23 mmol, yield 24%; **3j**: 104.1 mg, 0.32 mmol, yield 33%; **2k**: 75.5 mg, 0.22 mmol, yield 24 %; **3k**: 97.6 mg, 0.29 mmol, yield 31%.

Mixtures of ozonides **2a-k** + **3a-k** were isolated by chromatography on SiO_2 using PE : EA mixture as the eluent with a gradient of EA from 5 to 20 vol. %

Mixtures **2a + 3a**: 0.171 g, 0.79 mmol, yield 53%; **2b + 3b**: 0.231 g, 0.94 mmol, yield 72%; **2c + 3c**: 0.236 mg, 0.86 mmol, yield 74%; **2d + 3d**: 0.269 mg, 0.90 mmol, yield 85%; **2e+ 3e**: 0.243 mg, 0.95 mmol, yield 76%; **2f + 3f**: 0.114 g, 0.42 mmol, yield 36%; **2g + 3g**: 0.221 g, 0.69 mmol, yield 70%; **2h + 3h**: 0.285 mg, 0.84 mmol, yield 90%; **2i + 3i**: 0.275 g, 0.81 mmol, yield 87%; **2j + 3j**: 0.277 g, 0.85 mmol, yield 88%; **2k + 3k**: 0.240 g, 0.71 mmol, yield 76%;

Compounds **2a-g** and **3a-g** were previously described in detail in our previous papers.[16] Compounds **2h-k**, **3h-k** are new compounds.

Synthesis of ozonides from 1,5-diketone 1h in gram scale of 1h with use of PMA/SiO_2-(E).

A 7.4 M ethereal solution of H_2O_2 (0.624 mL, 4.61 mmol, 1.5 mol H_2O_2 / 1.0 mol of 1,5-diketone **1h**) and PMA/SiO_2-**(E)** (2.80 g, 10 wt.% $H_3PMo_{12}O_{40}$, 0.154 mmol of $H_3PMo_{12}O_{40}$, 0.05 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,5- diketone **1h**) were successively added to a stirred solution of 1,5-diketone **1h** (1.00 g; 3.07 mmol) in toluene (30 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1 h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump. Mixture of ozonides **2h** + **3h** was isolated by chromatography on SiO_2 using PE : EA mixture as the eluent with a gradient of EA from 5 to 20 vol. % Mixture of ozonides **2h** + **3h**: 0.596g, 1.75 mmol, yield 57%.

Synthesis of ozonides from 1,5-diketone 1h in gram scale of 1h with use of PMA/SiO_2-(G).

A 7.4 M ethereal solution of H_2O_2 (0.624 mL, 4.61 mmol, 1.5 mol H_2O_2 / 1.0 mol of 1,5-diketone **1h**) and PMA/SiO_2-**(G)** (2.80 g, 30 wt.% $H_3PMo_{12}O_{40}$, 0.460 mmol of $H_3PMo_{12}O_{40}$, 0.15 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,5- diketone **1h**) were successively added to a stirred solution of 1,5-diketone **1h** (1.00 g; 3.07 mmol) in toluene (30 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1 h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump. Mixture of ozonides **2h** + **3h** was isolated by chromatography on SiO_2 using PE : EA mixture as the eluent with a gradient of EA from 5 to 20 vol. % Mixture of ozonides **2h** + **3h**: 0.962g, 2.82 mmol, yield 92%.

Ethyl (1*R,2*S**,5*S**)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 2a[16a]**

Colorless oil. Yield 23%, 74.5 mg, 0.34 mmol. R_f = 0.38 (TLC, PE : EA, 20 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.27 (t, J = 7.1 Hz, 3H), 1.50 (s,

3H), 1.61 (s, 3H), 1.66-1.81 (m, 1H), 1.80-2.01 (m, 1H), 2.01-2.27 (m, 1H), 2.26-2.50 (m, 1H), 2.73 (d, J = 6.2 Hz, 1H), 4.03-4.29 (m, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), *δ*: 14.3, 20.5, 21.0, 21.1, 31.1, 46.8, 60.9, 108.1, 110.0, 171.3. The physical and spectral data were consistent with those previously reported.[16a]

Ethyl (1*S,2*S**,5*R**)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 3a[16a]**

White crystals. Mp = 50-51 °C (Lit.[16a] Mp = 49-50 °C). Yield 18%, 58.3 mg, 0.27 mmol. R_f = 0.34 (TLC, PE : EA, 20 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), *δ*: 1.26 (t, *J* = 7.1 Hz, 3H), 1.51 (s, 3H), 1.57 (s, 3H), 1.71-1.98 (m, 3H), 2.38-2.57 (m, 1H), 2.77 (dd, J = 12.3, 4.9 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H): ^{13}C NMR (75.48 MHz, $CDCl_3$), *δ*: 14.3, 20.4, 21.0, 21.3, 33.4, 49.4, 60.9, 107.7, 108.7, 171.6. The physical and spectral data were consistent with those previously reported.[16a]

Ethyl (1*R,2*S**,5*S**)-2-etyl-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 2b[16b]**

Colorless oil. Yield 35%, 112.4 mg, 0.46 mmol. R_f = 0.41 (TLC, PE : EA, 20 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), *δ*: 0.79 (t, *J* = 7.2 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.36-1.54 (m, 1H), 1.47 (s, 3H), 1.67 (s, 3H), 1.74-2.00 (m, 3H), 2.03-2.32 (m, 2H), 4.19 (q, *J* = 7.2 Hz, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), *δ*: 8.2, 14.3, 18.7, 20.6, 25.2, 28.1, 33.0, 53.7, 60.9, 109.6, 111.3, 172.9. The physical and spectral data were consistent with those previously reported.[16b]

Ethyl(1*S,2*S**,5*R**)-2-ethyl-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 3b[16b]**

Colorless oil. Yield 21%, 67.4 mg, 0.27 mmol. R_f = 0.35 (TLC, PE : EA, 20 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), *δ*: 0.84 (t, *J* = 7.4 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.48 (s, 3H), 1.58 (s, 3H), 1.62-2.01 (m, 5H), 2.59-2.73 (m, 1H), 4.16 (q, *J* = 7.4 Hz, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), *δ*: 9.3, 14.3, 18.9, 20.7, 21.7, 24.5, 31.1, 53.8, 61.0, 108.9, 111.4, 172.9. The physical and spectral data were consistent with those previously reported.[16b]

Ethyl(1*R,2*S**,5*S**)-2-butyl-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 2c[16b]**

Slightly yellow oil. Yield 38%, 121.1 mg, 0.44 mmol. R_f = 0.40 (TLC, PE : EA, 20 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), *δ*: 0.86 (t, *J* = 7.0 Hz, 3H), 0.80-1.06 (m, 1H), 1.18-1.34 (m, 3H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.35-1.53 (m, 1H), 1.46 (s, 3H), 1.67 (s, 3H), 1.72-1.97 (m, 3H), 2.05-2.19 (m, 2H), 4.11-4.25 (m, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), *δ*: 14.0, 14.3, 18.7, 20.6, 23.1, 25.7, 26.0, 33.0, 34.9, 53.3, 60.9, 109.6, 111.3, 173.0. The physical and spectral data were consistent with those previously reported.[16b]

Ethyl (1*S,2*S**,5*R**)-2-butyl-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 3c[16b]**

Colorless oil. Yield 24%, 76.5 mg, 0.28 mmol. R_f = 0.32 (TLC, PE : EA, 20 : 1); ^{1}H NMR (300.13 MHz, $CDCl_3$), *δ*: 0.89 (t, *J* = 7.1 Hz, 3H), 1.01-1.14 (m, 1H), 1.19-1.37 (m, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.48 (s, 3H), 1.57 (s, 3H), 1.61-1.91 (m, 5H), 2.59-2.73 (m, 1H), 4.14 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), *δ*: 14.0, 14.2, 18.9, 20.7, 22.4, 23.3, 27.2, 31.2, 31.4, 53.4, 61.0, 108.9, 111.4, 173.0. The physical and spectral data were consistent with those previously reported.[16b]

Ethyl (1*R,2*S**,5*S**)-2-hexyl-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 2d[16a]**

Slightly yellow oil. Yield 48%, 152.1 mg, 0.5 mmol. R_f = 0.43 (TLC, PE : EA, 5 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), *δ*: 0.86 (t, *J* = 6.7 Hz, 3H), 0.90-1.08 (m, 1H), 1.17-1.34 (m, 10H), 1.37-1.50 (m, 1H), 1.47 (s, 3H), 1.68 (s, 3H), 1.72-1.97 (m, 3H), 2.07-2.19 (m, 2H), 4.13-4.23 (m, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), *δ*: 14.1, 14.3, 18.8, 20.7, 22.7, 23.8, 25.7, 29.7, 31.7, 33.0, 35.2, 53.4, 60.9, 109.6, 111.3, 173.0. The physical and spectral data were consistent with those previously reported.[16a]

Ethyl (1*S,2*S**,5*R**)-2-hexyl-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 3d[16a]**

Colorless oil. Yield 22%, 69.7 mg, 0.23 mmol. R_f = 0.43 (TLC, PE : EA, 20 : 1); ^{1}H NMR (300.13 MHz, $CDCl_3$), *δ*: 0.78-0.94 (m, 3H), 0.96-1.36 (m, 11H), 1.49 (s, 3H), 1.58 (s, 3H), 1.61-1.90 (m, 5H), 2.58-2.77 (m, 1H), 4.15 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), *δ*: 14.2, 14.3, 18.9, 20.7, 22.4, 22.7, 25.0, 29.9, 31.2, 31.7, 31.8, 53.4, 61.0, 108.9, 111.4, 173.0. The physical and spectral data were consistent with those previously reported.[16a]

Ethyl (1*R,2*R**,5*S**)-2-allyl-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 2e[16a]**

Slightly yellow oil. Yield 40%, 128 mg, 0.5 mmol. R_f = 0.28 (TLC, PE : EA, 60 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), *δ*: 1.27 (t, *J* = 7.1 Hz, 3H), 1.47 (s, 3H), 1.68 (s, 3H), 1.72-2.23 (m, 5H), 2.62 (dd, *J* = 13.2, 6.8 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.99-5.14 (m, 2H), 5.50-5.70 (m, 1H); ^{13}C NMR (75.48 MHz, $CDCl_3$), *δ*: 14.3, 18.7, 20.7 26.0, 32.9, 39.8, 53.0, 61.1, 109.8, 110.9, 118.9, 132.4, 172.4. The physical and spectral data were consistent with those previously reported.[16a]

Ethyl (1*S,2*S**,5*R**)-2-allyl-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 3e[16a]**

Slightly yellow oil. Yield 23%, 73.6 mg, 0.28 mmol. R_f = 0.24 (TLC, PE : EA, 60 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), *δ*: 1.22 (t, *J* = 7.1 Hz, 3H), 1.50 (s, 3H), 1.57 (s, 3H), 1.61-1.83 (m, 3H), 2.48 (dd, *J* = 13.9, 8.7 Hz, 1H), 2.57-2.77 (m, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 5.03-5.14 (m, 2H), 5.54-5.72 (m, 1H); ^{13}C NMR (75.48 MHz, $CDCl_3$), *δ*: 14.3, 18.8, 20.8, 22.7, 30.8, 36.4, 52.8, 61.2, 109.0, 110.9, 118.7, 133.7, 172.6. The physical and spectral data were consistent with those previously reported.[16a]

Ethyl (1*R,2*S**,5*S**)-2-(2-cyanoethyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 2f[16a]**

White crystals. Mp = 83-84 °C (Lit.[16a] Mp = 83-84 °C). Yield 15%, 47.8 mg, 0.17 mmol. R_f = 0.61 (TLC, PE : EA, 5 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), *δ*: 1.31 (t, *J* = 7.1 Hz, 3H), 1.49 (s, 3H), 1.65 (s, 3H), 1.82-1.89 (m, 2H), 1.91-2.12 (m, 2H), 2.12-2.41 (m, 4H), 4.24 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), *δ*: 12.4, 14.2, 18.5, 20.5, 25.1, 30.8, 32.6, 52.2, 61.8, 109.7, 110.4, 118.9, 171.5. The physical and spectral data were consistent with those previously reported.[16a]

Ethyl (1*S,2*S**,5*R**)-2-(2-cyanoethyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 3f[16a]**

Colorless oil; Yield 13%, 41.4 mg, 0.15 mmol. R_f = 0.53 (TLC, PE : EA, 5 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), *δ*: 1.29 (t, *J* = 7.1 Hz, 3H), 1.52 (s, 3H), 1.53 (s, 3H), 1.61-1.72 (m, 1H), 1.78-1.93 (m, 2H), 2.14-2.45 (m, 4H), 2.75-2.89 (m, 1H), 4.20 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR (75.48 MHz,

$CDCl_3$), δ: 13.4, 14.2, 18.5, 20.6, 22.1, 27.1, 30.9, 52.7, 61.8, 109.0, 110.3, 119.4, 171.8. The physical and spectral data were consistent with those previously reported.[16a]

Ethyl (1*R,2*R**,5*S**)-2-(3-ethoxy-3-oxopropyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 2g[16b]**

Colorless oil. Yield 36%, 113.7 mg, 0.36 mmol. R_f = 0.43 (TLC, PE : EA, 5 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.23 (t, J = 7.1 Hz, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.46 (s, 3H), 1.68 (s, 3H), 1.71-2.36 (m, 8H), 4.10 (q, J = 7.1 Hz, 2H), 4.18 (q, J = 7.1 Hz, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.2, 14.3, 18.7, 20.6, 25.4, 29.1, 30.1, 32.8, 52.5, 60.7, 61.3, 109.6, 110.0, 172.3, 172.9. The physical and spectral data were consistent with those previously reported.[16b]

Ethyl (1*S,2*R**,5*R**)-2-(3-ethoxy-3-oxopropyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 3g[16b]**

Colorless oil. Yield 23%, 72.6 mg, 0.23 mmol. R_f = 0.31 (TLC, PE : EA, 5 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.18-1.32 (m, 6H), 1.48 (s, 3H), 1.56 (s, 3H), 1.53-1.63 (m, 1H), 1.72-1.87 (m, 2H), 2.05-2.29 (m, 4H), 2.63-2.77 (m, 1H), 4.04-4.22 (m, 4H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.2, 14.3, 18.8, 20.6, 22.4, 26.4, 30.2, 30.9, 52.7, 60.7, 61.3, 108.9, 110.9, 172.4, 173.1. The physical and spectral data were consistent with those previously reported.[16b]

Ethyl (1*R,2*R**,5*S**)-2-(4-chlorobenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 2h**

White crystals. Mp = 99-100 °C. Yield 21%, 66.0 mg, 0.19 mmol. R_f = 0.46 (TLC, PE : EA, 10 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.26 (t, J = 7.1 Hz, 3H), 1.48 (s, 3H), 1.56-1.82 (m, 2H), 1.79 (s, 3H), 1.90-2.12 (m, 2H), 2.60 (d, J = 12.9 Hz, 1H), 3.31 (d, J = 12.9 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 7.0 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.2 Hz, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.2, 18.7, 20.6, 25.7, 32.9, 40.3, 54.2, 61.3, 109.9, 111.1, 128.5, 131.3, 132.9, 134.6, 172.3. Anal. Calcd for $C_{17}H_{21}ClO_5$: C, 59.91; H, 6.21; Cl, 10.40. Found: C, 59.94; H, 6.22; Cl, 10.38; HRMS (ESI-TOF): m/z $[M+Na]^+$: calculated for $[C_{17}H_{21}ClNaO_5]^+$: 363.0970; found: 363.0981.

Ethyl (1*S,2*R**,5*R**)-2-(4-bromobenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 3h**

White crystals. Mp = 89-90 °C. Yield 24%, 75.5 mg, 0.22 mmol. R_f = 0.40 (TLC, PE : EA, 10 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.23 (t, J = 7.1 Hz, 3H), 1.47 (ddd, J = 14.4, 5.3, 2.3 Hz, 1H), 1.56 (s, 3H), 1.66 (s, 3H), 1.76-1.97 (m, 2H), 2.61 (td, J = 13.2, 6.5 Hz, 1H), 3.01 (d, J = 13.7 Hz, 1H), 3.33 (d, J = 13.7 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 7.04 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.2, 19.1, 20.8, 21.8, 31.2, 37.0, 54.4, 61.4, 109.2, 111.3, 128.6, 131.4, 132.9, 135.8, 172.4. Anal. Calcd for $C_{17}H_{21}ClO_5$: C, 59.91; H, 6.21; Cl, 10.40. Found: C, 59.93; H, 6.21; Cl, 10.39; HRMS (ESI-TOF): m/z $[M+Na]^+$: calculated for $[C_{17}H_{21}ClNaO_5]^+$: 363.0970; found: 363.0973.

Ethyl (1*R,2*R**,5*S**)-2-(3-chlorobenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 2i**

Slightly yellow oil. Yield 28%, 88.0 mg, 0.26 mmol. R_f = 0.53 (TLC, PE : EA, 10 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.27 (t, J = 7.0 Hz, 3H), 1.49 (s, 3H), 1.55-1.87 (m, 2H), 1.80 (s, 3H), 1.90-2.16 (m, 2H), 2.60 (d, J = 12.8 Hz, 1H), 3.31 (d, J = 12.8 Hz, 1H), 4.21 (q, J = 7.0 Hz, 2H), 6.87-7.23 (m, 4H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.2, 18.7, 20.6, 25.7, 32.9, 40.7, 54.1, 61.3, 109.9, 111.0, 127.1, 128.2, 129.6, 130.0, 134.2, 138.2, 172.3. Anal. Calcd for $C_{17}H_{21}ClO_5$: C, 59.91; H, 6.21; Cl, 10.40. Found: C, 59.92; H, 6.20; Cl, 10.38; HRMS (ESI-TOF): m/z $[M+Na]^+$: calculated for $[C_{17}H_{21}ClNaO_5]^+$: 363.0970; found: 363.0973.

Ethyl (1*S,2*R**,5*R**)-2-(3-chlorobenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2 carboxylate, 3i**

Slightly yellow oil; Yield 30%, 94.3 mg, 0.27 mmol.; R_f = 0.49 (TLC, PE : EA, 10 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.24 (t, J = 7.0 Hz, 3H), 1.56 (s, 3H), 1.67 (s, 3H), 1.40-1.72 (m, 1H), 1.74-1.99 (m, 2H), 2.52-2.72 (m, 1H), 3.01 (d, J = 13.6 Hz, 1H), 3.33 (d, J = 13.6 Hz, 1H), 4.16 (q, J = 7.0 Hz, 2H), 6.90-7.24 (m, 4H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.2, 19.1, 20.8, 21.8, 31.2, 37.3, 54.3, 61.5, 109.3, 111.3, 127.2, 128.3, 129.7, 130.2, 134.3, 139.3, 172.4. Anal. Calcd for $C_{17}H_{21}ClO_5$: C, 59.91; H, 6.21; Cl, 10.40. Found: C, 59.93; H, 6.23; Cl, 10.39; HRMS (ESI-TOF): m/z $[M+Na]^+$: calculated for $[C_{17}H_{21}ClNaO_5]^+$: 363.0970; found: 363.0974.

Ethyl (1*R,2*R**,5*S**)-2-(4-fluorobenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 2j**

Slightly yellow oil; Yield 24%, 75.7 mg, 0.23 mmol. R_f = 0.61 (TLC, PE : EA, 10 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.26 (t, J = 7.1 Hz, 3H), 1.48 (s, 3H), 1.56-1.84 (m, 2H), 1.80 (s, 3H), 1.90-2.12 (m, 2H), 2.60 (d, J = 13.0 Hz, 1H), 3.30 (d, J = 13.0 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 6.88-7.07 (m, 4H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.2, 18.7, 20.6, 25.7, 32.9, 40.2, 54.2, 61.2, 109.8, 111.1, 115.2 (d, $^2J_{CF}$ = 21.1 Hz), 131.4 (d, $^3J_{CF}$ = 7.8 Hz), 131.8 (d, $^4J_{CH}$ = 3.3 Hz), 162.0 (d, $^1J_{CF}$ = 244.9 Hz), 172.4. Anal. Calcd for $C_{17}H_{21}FO_5$: C, 62.95; H, 6.53; F, 5.86. Found: C, 62.97; H, 6.55; F, 5.84; HRMS (ESI-TOF): m/z $[M+Na]^+$: calculated for $[C_{17}H_{21}FNaO_5]^+$: 347.1265; found: 347.1250.

Ethyl (1*S,2*R**,5*R**)-2-(4-fluorobenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 3j**

White crystals. Mp = 57-58 °C. Yield 33%, 104.1 mg, 0.32 mmol. R_f = 0.54 (TLC, PE : EA, 10 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.22 (t, J = 7.1 Hz, 3H), 1.56 (s, 3H), 1.43-1.59 (m, 1H), 1.67 (s, 3H), 1.74-2.05 (m, 2H), 2.52-2.67 (m, 1H), 3.01 (d, J = 13.7 Hz, 1H), 3.32 (d, J = 13.7 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 6.88-7.11 (m, 4H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.2, 19.1, 20.8, 21.7, 31.1, 36.8, 54.5, 61.4, 109.2, 111.3, 115.3 (d, $^2J_{CF}$ = 21.2 Hz), 131.5 (d, $^3J_{CF}$ = 7.9 Hz), 131.9 (d, $^4J_{CH}$ = 3.4 Hz), 162.0 (d, $^1J_{CF}$ = 245.4 Hz) 172.5. Anal. Calcd for $C_{17}H_{21}FO_5$: C, 62.95; H, 6.53; F, 5.86. Found: C, 62.96; H, 6.53; F, 5.84; HRMS (ESI-TOF): m/z $[M+Na]^+$: calculated for $[C_{17}H_{21}FNaO_5]^+$: 347.1265; found: 347.1262.

Ethyl (1*R,2*R**,5*S**)-2-(3-methoxybenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 2k**

Slightly yellow oil. Yield 24%, 75.5 mg, 0.22 mmol. R_f = 0.58 (TLC, PE : EA, 10 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.27 (t, J = 7.1 Hz, 3H), 1.48 (s, 3H), 1.62-1.84 (m, 2H), 1.81 (s, 3H), 1.93-2.13 (m, 2H), 2.59 (d, J = 12.8 Hz, 1H), 3.33 (d, J = 12.8 Hz, 1H), 3.76 (s, 3H), 4.20 (q, J = 7.1 Hz, 2H), 6.60-6.69 (m, 2H), 6.72-6.79 (m, 1H), 7.15 (t, J = 7.9 Hz, 1H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.2, 18.7, 20.6, 25.7, 32.9, 41.0, 54.2, 55.2, 61.1, 109.9, 111.2, 112.3, 115.7, 122.3, 129.2, 137.6, 159.5, 172.5. Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.26; H, 7.21. HRMS (ESI-TOF): m/z $[M+Na]^+$: calculated for $[C_{18}H_{24}NaO_6]^+$: 359.1465; found: 359.1455.

Ethyl (1*S,2*R**,5*R**)-2-(3-methoxybenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octane-2-carboxylate, 3k**

White crystals. Mp = 76-78 °C. Yield 31%, 97.6 mg, 0.29 mmol. R_f = 0.53 (TLC, PE : EA, 10 : 1). ^{1}H NMR (300.13 MHz, $CDCl_3$), δ: 1.23 (t, J = 7.1 Hz, 3H), 1.46-1.58 (m, 1H), 1.55 (s, 3H), 1.67 (s, 3H), 1.73-1.98 (m, 2H), 2.60 (td, J = 13.3 Hz, J = 6.3 Hz, 1H), 3.00 (d, J = 13.5 Hz, 1H), 3.34 (d, J = 13.5 Hz, 1H), 3.75 (s, 3H), 4.15 (q, J = 7.1 Hz, 2H), 6.63-6.71 (m, 2H), 6.72-6.79 (m, 1H), 7.16 (t, J = 7.9 Hz, 1H); ^{13}C NMR (75.48 MHz, $CDCl_3$), δ: 14.1, 19.1, 20.8, 21.8, 31.2, 37.7, 54.3, 55.2, 61.3, 109.2, 111.4, 112.0, 115.9, 122.4, 129.3, 138.7, 159.6, 172.6. Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.25; H, 7.20. HRMS (ESI-TOF): m/z $[M+Na]^+$: calculated for $[C_{18}H_{24}NaO_6]^+$: 359.1465; found: 359.1471.

Procedure for peroxidation of 4d with use of 7.4 M ethereal solution of H_2O_2 and PMA/SiO_2-(E) (Table 3, Runs 1, 4, and 5)

A 7.4 M ethereal solution of H_2O_2 (0.864 mL, 1.38 mmol, 3.0 mol H_2O_2 / 1.0 mol of **4d**) and PMA/SiO_2-**(E)** (1.750 – 5.255 g, 10 wt.% $H_3PMo_{12}O_{40}$, 0.096 – 0.288 mmol of $H_3PMo_{12}O_{40}$, 0.05-0.15 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,3- diketone **4d**) were successively added to a stirred solution of 1,3-diketone **4d** (0.300 g; 1.92 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1 h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump. Tetraoxane **5d** was isolated by chromatography on SiO_2 using PE : EA (10 : 1).

Procedure for peroxidation of 4d with use of 7.4 M ethereal solution of H_2O_2 and PMA/SiO_2-(F) (Table 3, Run 2)

A 7.4 M ethereal solution of H_2O_2 (0.864 mL, 1.38 mmol, 3.0 mol H_2O_2 / 1.0 mol of **4d**) and PMA/SiO_2-**(F)** (0.875 g, 20 wt.% $H_3PMo_{12}O_{40}$, 0.096 mmol of $H_3PMo_{12}O_{40}$, 0.05 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,3- diketone **4d**) were successively added to a stirred solution of 1,3-diketone **4d** (0.300 g; 1.92 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1 h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump. Tetraoxane **5d** was isolated by chromatography on SiO_2 using PE : EA (10 : 1).

Procedure for peroxidation of 4d with use of 7.4 M ethereal solution of H_2O_2 and PMA/SiO_2-(G) (Table 3, Runs 3, 6)

A 7.4 M ethereal solution of H_2O_2 (0.864 mL, 1.38 mmol, 3.0 mol H_2O_2 / 1.0 mol of **4d**) and PMA/SiO_2-**(G)** (0.584 – 1.168 g, 30 wt.% $H_3PMo_{12}O_{40}$, 0.096 – 0.192 mmol of $H_3PMo_{12}O_{40}$, 0.05 – 0.10 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,3- diketone **4d**) were successively added to a stirred solution of 1,3-diketone **4d** (0.300 g; 1.92 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1 h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump. Tetraoxane **5d** was isolated by chromatography on SiO_2 using PE : EA (10 : 1).

Synthesis of tetraoxane 5f from 1,3-diketone 4f in gram scale of 4f with the use of PMA/SiO_2-(G)

A 7.4 M ethereal solution of H_2O_2 (2.38 mL, 17.62 mmol, 3.0 mol H_2O_2 / 1.0 mol of **4f**) and PMA/SiO_2-**(G)** (3.57 g, 30 wt.% $H_3PMo_{12}O_{40}$, 0.59 mmol of $H_3PMo_{12}O_{40}$, 0.10 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,3- diketone **4f**) were successively added to a stirred solution of 1,3-diketone **4f** (1.000 g; 5.87 mmol) in toluene (30 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1 h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump. Tetraoxane **5f** was isolated by chromatography on SiO_2 using PE : EA (10 : 1). Tetraoxane **5f**: 0.712g, 3.52 mmol, yield 60%.

General procedure for the synthesis of tetraoxanes from diketones 5a-k

A 7.4 M ethereal solution of H_2O_2 (0.454 – 1.066 mL, 3.36 – 7.89 mmol, 3.0 mol H_2O_2 / 1.0 mol of **4a-k**) and PMA/SiO_2-**(G)** (0.682 – 1.600 g, 30 wt.% $H_3PMo_{12}O_{40}$, 0.112 - 0.263 mmol of $H_3PMo_{12}O_{40}$, 0.10 mol $H_3PMo_{12}O_{40}$ / 1.0 mol 1,3- diketone **4f**) were successively added to a stirred solution of 1,3-diketone **4a-k** (0.300 g; 1.12 - 2.63 mmol) in toluene (10 mL) at 20-25 °C. The reaction mixture was stirred at 20-25°C for 1 h. After that time the catalyst was filtered off and washed with CH_2Cl_2 (3 × 10 ml). The solvent was removed in vacuum of a water jet pump. Tetraoxanes **5a-k** were isolated by chromatography on SiO_2 using PE : EA (10 : 1). Tetraoxane **5f**: 0.712g, 3.52 mmol, yield 60%.

Compounds: **5a**: 222.7 mg, 1.52 mmol, yield 58%; **5b**: 224.9 mg, 1.40 mmol, yield 60%; **5c**: 206.3 mg, 1.19 mmol, yield 56%; **5d**: 231.3 mg, 1.23 mmol, yield 64%; **5e**: 245.9 mg, 1.21 mmol, yield 69%; **5f**: 224.5 mg, 1.11 mmol, yield 63%; **5g**: 207.7 mg, 0.96 mmol, yield 59%; **5h**: 252.0 mg, 1.03 mmol, yield 73%; **5i**: 226.0 mg, 0.97 mmol, yield 65%; **5j**: 293.2 mg, 1.1 mmol, yield 86%; **5k**: 273.0 mg, 0.90 mmol, yield 81%;

1,4,7-Trimethyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane, 5a[11g]

Slightly yellow crystals. Mp = 55-56 °C (Lit.[11g] Mp = 56 °C). Yield 58%, 222.7 mg, 1.52 mmol. R_f = 0.31 (TLC, PE : EA, 10:1). ^{1}H NMR (300.13 MHz, $CDCl_3$) δ: 1.18 (d, J = 6.7 Hz, 3H), 1.52 (s, 6H), 2.77 (q, J = 6.7 Hz, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ: 8.3, 9.4, 54.4, 110.8. The physical and spectral data were consistent with those previously reported.[11g]

7-Ethyl-1,4-dimethyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane, 5b[11g]

Slightly yellow oil. Yield 60%, 224.9 mg, 1.40 mmol. R_f = 0.53 (TLC, PE : EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$) δ: 1.11 (t, J = 6.3 Hz, 3H,), 1.55 (s, 6H), 1.61-1.68 (m, 2H), 2.56 (t, J = 6.3 Hz, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ: 10.0, 12.3, 17.2, 60.9, 110.9. The physical and spectral data were consistent with those previously reported.[11g]

7-Allyl-1,4-dimethyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane, 5c[11a]

Slightly yellow oil. Yield 56%, 206.3 mg, 1.19 mmol. R_f = 0.56 (TLC, PE : EA, 10:1).^{1}H NMR (300.13 MHz, $CDCl_3$) δ: 1.53 (s, 6H), 2.38 (t, J = 6.7 Hz, 2H), 2.78 (t, J = 6.7 Hz, 1H), 5.15-5.20 (m, 2H), 5.80-5.93 (m, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ: 10.0, 28.6, 57.9, 110.7, 118.0, 134.1. The physical and spectral data were consistent with those previously reported.[11a]

7-Butyl-1,4-dimethyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane, 5d[11a]

Slightly yellow oil. Yield 64%, 231.3 mg, 1.23 mmol. R_f = 0.68 (TLC, PE : EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$) δ: 0.93 (t, J = 7.0 Hz, 3H), 1.30 – 1.53 (m, 4H), 1.55 (s, 6H), 1.57 – 1.61 (m, 2H), 2.60 (t, J = 5.9 Hz, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ: 9.9, 13.9, 22.9, 23.7, 29.9, 59.2, 110.9. The physical and spectral data were consistent with those previously reported.[11a]

1,4-Dimethyl-7-pentyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane, 5e

Slightly yellow oil. Yield 69%, 245.9 mg, 1.21 mmol. R_f = 0.64 (TLC, PE : EA, 10:1). ^{1}H NMR (300.13 MHz, $CDCl_3$) δ: 0.91 (t, J = 7.0 Hz, 3H), 1.34 – 1.37 (m, 4H), 1.46 – 1.48 (m, 2H), 1.54 (s, 6H), 1.55 – 1.62 (m, 2H), 2.62 (t, J = 5.8 Hz, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ: 10.0, 14.1, 22.5, 24.0, 27.5, 32.1, 59.3, 111.0. Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.39; H, 8.97.

Found: C, 59.40; H, 8.98. HRMS (ESI-TOF): m/z $[M+H]^+$: calculated for $[C_{10}H_{18}O_4]^+$: 203.1278; found: 203.1287.

7-Isopentyl-1,4-dimethyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane, 5f

Slightly yellow oil. Yield 63%, 224.5 mg, 1.11 mmol. R_f = 0.60 (TLC, PE : EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$) *δ*: 0.93 (d, *J* = 6.6 Hz, 6H), 1.30 – 1.40 (m, 2H), 1.54 (s, 6H), 1.50-1.64 (m, 3H) 2.59 (t, *J* = 6.6 Hz, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$) *δ*: 10.0, 21.9, 22.5, 28.4, 36.9, 59.5, 110.9 Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.39; H, 8.97. Found: C, 59.41; H, 8.97. HRMS (ESI-TOF): m/z $[M+H]^+$: calculated for $[C_{10}H_{19}O_4]^+$: 203.1278; found: 203.1270.

7-Hexyl-1,4-dimethyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane, 5g[11c]

Slightly yellow oil. Yield 59%, 207.7 mg, 0.96 mmol. R_f = 0.67 (TLC, PE : EA, 10:1). ^{1}H NMR (300.13 MHz, $CDCl_3$) *δ*: 0.92 (t, *J* = 7.0 Hz, 3H), 1.27 – 1.41 (m, 6H), 1.43 – 1.54 (m, 2H), 1.56 (s, 6H), 1.58 – 1.54 (m, 2H), 2.64 (t, *J* = 5.9 Hz, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$) *δ*: 10.0, 14.2, 22.7, 24.0, 27.8, 29.6, 31.7, 59.3, 111.0.The physical and spectral data were consistent with those previously reported.[11c]

1,4-Dimethyl-7-octyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane, 5h

Slightly yellow oil. Yield 73%, 252.0 mg, 1.03 mmol. R_f = 0.5 (TLC, PE : EA, 20:1). ^{1}H NMR (300.13 MHz, $CDCl_3$) *δ*: 0.88 (t, *J* = 7.0 Hz, 3H), 1.20 – 1.35 (m, 10H), 1.54 (s, 6H), 1.46 – 1.58 (m, 4H), 2.61 (t, *J* = 5.8 Hz, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$) *δ*: 10.0, 14.2, 22.8, 24.0, 27.8, 29.3, 29.4, 29.9, 31.9, 59.3, 111.0. Anal. Calcd for $C_{13}H_{24}O_4$: C, 63.91; H, 9.90. Found: C, 63.92; H, 9.91. HRMS (ESI-TOF): m/z $[M+K]^+$: calculated for $[C_{13}H_{24}KO_4]^+$: 283.1306; found: 283.1307.

Ethyl 3-(1,4-dimethyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptan-7-yl)propanoate, 5i[11a]

Slightly yellow oil. Yield 65%, 226.0 mg, 0.97 mmol. R_f = 0.50 (TLC, PE : EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$) *δ*: 1.21 (t, *J* = 7.1 Hz, 3H), 1.50 (s, 6H), 1.84 (q, *J* = 7.3 Hz, 2H), 2.44 (t, *J* = 7.3 Hz, 2H), 2.63 (t, *J* = 5.9 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H). ^{13}C NMR (75.48 MHz, $CDCl_3$) *δ*: 9.7, 14.2, 19.0, 31.7, 58.1, 60.7, 110.7, 172.3. The physical and spectral data were consistent with those previously reported.[11a]

7-(Adamantan-1-yl)-1,4-dimethyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane, 5j[11a]

White crystals. Mp = 131-132 °C (Lit.[3c] Mp = 130 – 131 °C). Yield 86%, 293.2 mg, 1.52 mmol. R_f = 0.67 (TLC, PE : EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$) *δ*: 1.68-2.04 (m, 21H), 2.40 (s, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$) *δ*: 12.8, 28.5, 33.1, 36.9, 40.8, 67.0, 110.7. The physical and spectral data were consistent with those previously reported.[11a]

7-(4-Bromophenyl)-1,4-dimethyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane, 5k

White crystals. Mp = 121-123 °C. Yield 81%, 273.0 mg, 0.90 mmol. R_f =0.5 (TLC, PE : EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$) *δ*: 1.39 (s, 6H), 2.90 (d, *J* = 7.2 Hz, 2H), 3.06 (t, *J* = 7.2 Hz, 1H), 7.16 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR (75.48 MHz, $CDCl_3$) *δ*: 10.0, 29.9, 59.14, 110.7, 121.0, 130.6, 132.1, 136.4. Anal. Calcd for $C_{12}H_{13}BrO_4$: C, 47.86; H, 4.35; Br, 26.53 Found: C, 47.63; H, 4.41; Br, 26.74. HRMS (ESI-TOF): m/z $[M+K]^+$: calculated for $[C_{12}H_{13}BrKO_4]^+$: 338.9629; found: 338.9635.

Bioassay of fungicidal activity

The antifungal activities were tested according to the conventional procedure[48] with 15 phytopathogenic fungi from different taxonomic classes: *Venturia inaequalis (V.i.), Rhizoctonia solani (R.s.), Fusarium oxysporum (F.o.), Fusarium moniliforme (F.m.), Bipolaris sorokiniana (B.s.), Sclerotinia sclerotiorum (S.s.), Fusarium graminearum (F.g.), Fusarium heterosporum (F.h.), Fusarium culmorum (F.c.), Fusarium gibbosum (F.gb.), Fusarium nivale (Microdochium nivale) (F.m.n.), Fusarium sporotrichiella (F.s.), Alternaria alternata (A.), Pythium graminicola (P. sp.), Phoma eupyrena (P.e.).* The effect of the chemicals on mycelial radial growth was determined by dissolving concentration 3 mg×mL^{-1} in acetone and suspending aliquots in potato-saccharose agar at 50 °C to give the concentration (0.3-30 μg×mL^{-1}. The final acetone concentration of both fungicide-containing and control samples was 10 mL×L^{-1}. Petri dishes containing 15 mL of the agar medium were inoculated by placing 2-mm micelial agar discs on the agar surface. Plates were incubated at 25 °C and radial growth was measured after 72 h. The mixed medium without sample was used as the blank control. Three replicates of each test were carried out. The mycelium elongation diameter (mm) of fungi settlements was measured after 72 h of culture. The growth inhibition rates were calculated with the following equation: $I = [(D_C - D_T)/D_C] \times 100\%$. Here *I* is the growth inhibition rates (%), D_C is the control settlement diameter (mm), and D_T is the treatment group fungi settlement diameter (mm). Commercially available agricultural fungicide Triadimefon and Kresoxim-methyl were used as positive controls. EC_{50} values were calculated by non-linear regression using an equation for a sigmoidal dose-response curve with variable slope (Prism 7.0, GraphPad Software, San Diego).

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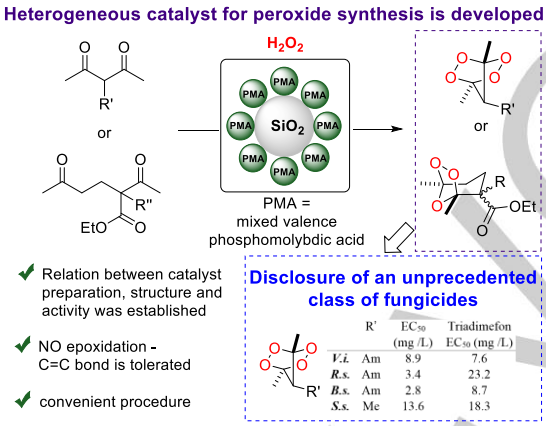
FULL PAPER

The catalyst was developed for peroxidation of 1,3- and 1,5-diketones with hydrogen peroxide with the formation of bridged 1,2,4,5-tetraoxanes and bridged 1,2,4-trioxolanes with yield up to 86 and 90% respectively based on isolated product under heterogeneous conditions. A new class of antifungal agents for crop protection, cyclic peroxides, was discovered. Some ozonides and tetraoxanes exhibit a very high antifungal activity and are superior to commercial agro fungicides.



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Catalyst development for the synthesis of ozonides and tetraoxanes under heterogeneous conditions. Disclosure of an unprecedented class of fungicides for agricultural application