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Synthesis of Peroxides from β,δ-Triketones under Heterogeneous Conditions

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Abstract—Heterogeneous reactions of β,δ-triketones with ethereal hydrogen peroxide in nonpolar solvents, catalyzed by phosphomolybdic acid, afforded mixtures of stereoisomeric ozonides, tricyclic monoperoxides, and bridged tetraoxanes. The trioxolane ring is formed by the carbonyl groups located in the δ-position with respect to each other.

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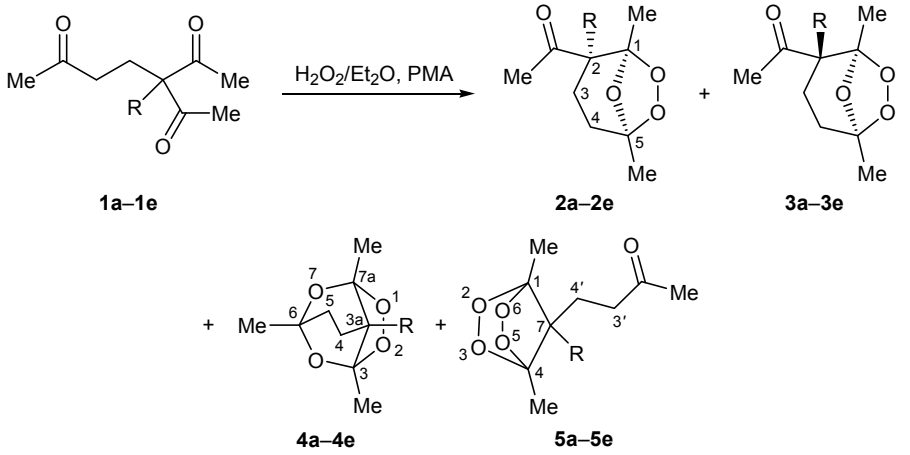
The chemistry of organic peroxides is largely based on reactions of carbonyl compounds, i.e., ketones and aldehydes, with hydrogen peroxide and hydroperoxides [1, 2]. Aldehydes and ketones are accessible compounds, and they readily react through the carbonyl carbon atom with highly nucleophilic hydroperoxide oxygen atom. In recent time, the chemistry of organic peroxides has developed especially vigorously since some of them have been found to exhibit antimalarial [3–6] and antihelminthic activity [7–9]. Natural peroxide artemisinin and its semisynthetic derivatives (artemether, arteether, and artesunate) have been used over several decades for the treatment of malaria [10].

Organic peroxides are produced on a large-scale from ketones and are used as radical polymerization initiators [11, 12] and cross-linking agents [13, 14]. The need of low-cost and efficient radical initiators, as well as of biologically active peroxides stimulates development of new methods of synthesis of peroxides from ketones and their derivatives with the use of hydrogen peroxide and hydroperoxides [15–25]. Peroxidation of monocarbonyl compounds has been studied in detail [15–21]. Considerably less data are available on the peroxidation of di- and tricarbonyl compounds with hydrogen peroxide [22–26]; these reactions are often nonselective and provide low yields.

Scheme 1.



R = $PhCH_2$ (**a**), 4-$O_2NC_6H_4CH_2$ (**b**), 4-$MeC_6H_4CH_2$ (**c**), 4-$ClC_6H_4CH_2$ (**d**), 4-$BrC_6H_4CH_2$ (**e**).

In the present study we have shown that phosphomolybdic acid catalyzes peroxidation of β,δ-triketones under heterogeneous conditions with formation of mixtures of three types of peroxides, namely ozonides, tricyclic monoperoxides, and bridged tetraoxanes. Heterogeneous conditions allow the catalyst to be recycled, considerably simplify the isolation procedure, and make the process more economic.

Peroxidation of β,δ-triketones **1a**–**1e** with a solution of hydrogen peroxide in diethyl ether, catalyzed by phosphomolybdic acid (PMA), in benzene, toluene, or carbon tetrachloride led to the formation of stereoisomeric ozonides **2a**–**2e** and **3a**–**3e**, tricyclic monoperoxides **4a**–**4e**, and bridged tetraoxanes **5a**–**5e** (Scheme 1). The effects of the amount of the catalyst and solvent nature on the product yields and ratio was studied in the peroxidation of 3-acetyl-3-benzylheptane-2,6-dione (**1a**) (see table). The reaction of **1a** with H_2O_2/Et_2O in the presence of PMA in benzene, toluene, and CCl_4 afforded a mixture of steroisomeric peroxides **2a** and **3a**, tricyclic monoperoxide **4a**, and tetraoxane **5a** (see table, run nos. 1–10); the yields were comparable with those obtained under homogeneous conditions [26]. The use of preliminarily modified catalyst favored formation of **4a** and **5a** in higher yields (run nos. 3, 7) than in the reaction with commercial PMA. The catalyst morphology was studied by field-emission scanning electron microscopy (FESEM; see figure).

It was presumed that thermal treatment of commercial phosphomolybdic acid hydrate ($H_3PMo_{12}O_{40} \cdot n H_2O$) removes crystallization water, which opens active sites for the interactions with hydrogen peroxide and carbonyl groups of β,δ-triketone and increases porosity and specific surface area of the catalyst.

Likewise, heterogeneous peroxidation of β,δ-triketones **1b**–**1e** with H_2O_2 gave mixtures of stereoisomeric ozonides **2b**–**2e** and **3b**–**3e**, tricyclic monoperoxides **4b**–**4e**, and bridged tetraoxanes **5b**–**5e**.

The described reaction may be regarded as a novel unique one-pot method of synthesis of three different peroxides whose preparation by known methods requires more complicated experimental procedures. The trioxolane ring in **2** and **3** is formed from two carbonyl groups occurring in the δ position with respect to each other, whereas the formation of tetraoxanes **5** involves the β-dicarbonyl fragment of the substrate. The resulting peroxides can be separated by column chromatography on silica gel. It was surprising that one carbonyl group of initial β,δ-triketones **1** remained unchanged in the described transformation, since just carbonyl functionality is generally highly reactive toward hydrogen peroxide. We have found only one reference to and one publication on the synthesis of ozonides from ketones [27, 28].

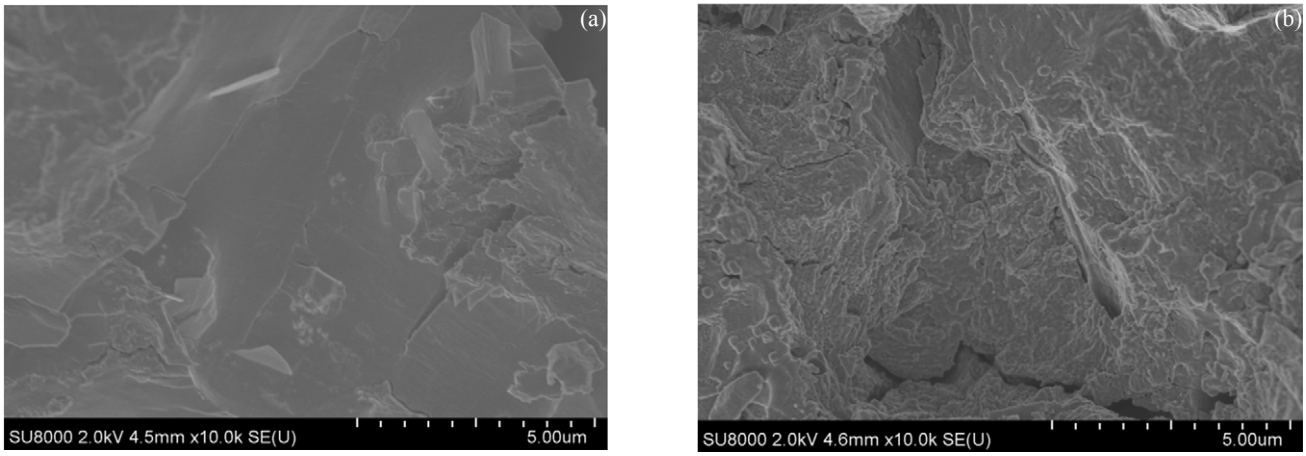
The scientific novelty of the peroxidation of organic compounds with hydrogen peroxide consists of the use of solid catalysts (metal salts) under heterogeneous conditions. Heterogeneous peroxidation is more advantageous than homogeneous catalysis due to the possibility for recycling of the catalyst without additional regeneration procedure or utilization after single application. Furthermore, the proposed proce-

Synthesis of peroxides **2a**–**5a** from triketone **1a** and H_2O_2

Run no.	Reaction time, h	Co-solvent	Yield,[a] %			
			2a	**3a**	**4a**	**5a**
1	8	Benzene	10	8	15	17
2	24	Benzene	10	10	15	18
3[b]	8	Benzene	12	10	26	27
4[b]	24	Benzene	10	11	29	27
5	8	Toluene	11	9	21	20
6	24	Toluene	11	8	22	22
7[b]	8	Toluene	14 (11)	11 (9)	28 (25)	29 (24)
8[b]	24	Toluene	12	12	28	31
9	8	Carbon tetrachloride	9	9	35	26
10[b]	8	Carbon tetrachloride	7	8	29	21

[a] According to the NMR data; isolated yield is given in parentheses.

[b] Phosphomolybdic acid was preliminarily dissolved in ethanol (10 mL), the solvent was distilled off, and the residue was heated for 2 h at 120°C under atmospheric pressure.



FESEM images of phosphomolybdic acid: (a) commercial sample and (b) after treatment.

dure is economic and more compliable to the "green chemistry" principles. Its experimental simplicity provides the basis for large-scale syntheses of peroxides.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AM 300 spectrometer at 300.13 and 75.48 MHz, respectively, using $CDCl_3$ as solvent. The procedure for FESEM study was described in [29]. The melting points were measured on a Kofler hot stage. Silica gel (0.060–0.200 mm, 60 Å, CAS no. 7631-86-9) was used for column chromatography. Benzene, toluene, carbon tetrachloride, petroleum ether (bp 40–70°C), ethyl acetate, phosphomolybdic acid hydrate (80%), acetylacetone, methyl vinyl ketone, alkyl bromides, and sodium sulfate were commercial products (Acros Organics). A solution of hydrogen peroxide in diethyl ether (5.8 wt %) was prepared by extraction of 37% aq. H_2O_2 (100 mL) with Et_2O (5×100 mL), followed by drying of the extract over $MgSO_4$. β,δ-Triketones **1a** [30] and **1b**–**1e** [31] were synthesized according to known procedures.

Treatment of the catalyst. Commercial phosphomolybdic acid was dissolved in 10 mL of ethanol, the solvent was distilled off, and the residue was heated for 2 h at 120°C under atmospheric pressure. The originally yellow sample turned green and lost 20% of the initial weight.

Peroxidation of 3-acetyl-3-benzylheptane-2,6-dione (1a) over phosphomolybdic acid. *a* (See table; run nos. 1, 2, 5, 6, 9). A solution of hydrogen peroxide in diethyl ether (1.57 mL, 1.73 mmol, c = 1.10 M; 1.5 mol of H_2O_2 per mole of **1a**) and 0.26 g (10 mol %) of commercial PMA were added in succession under stirring at 20–25°C to a solution of 0.30 g (1.15 mmol) of triketone **1a** in 4 mL of benzene, toluene, or carbon tetrachloride. The mixture was stirred for 8 h (24 h in run nos. 2, 6) at 20–25°C and applied to a column charged with silica gel (1×10 cm), and the sorbent was eluted with petroleum ether–ethyl acetate (1:3). The solvent was removed under reduced pressure (watr-jet pump), and the yields of **2a**–**5a** were determined by NMR.

b (See table; run nos. 3, 4, 7, 8, 10). A solution of hydrogen peroxide in diethyl ether (1.57 mL, 1.73 mmol, c = 1.10 M; 1.5 mol of H_2O_2 per mole of **1a**) and 0.21 g (10 mol %) of preliminarily treated PMA were added in succession under stirring at 20–25°C to a solution of 0.30 g (1.15 mmol) of triketone **1a** in 4 mL of benzene, toluene, or carbon tetrachloride. The mixture was stirred for 8 h (24 h in run nos. 4, 8) at 20–25°C, the solution was separated from the catalyst by decanting, and the catalyst (which resided on the walls of the flask due to its high adhesion to glass) was washed with the corresponding solvent (2×2 mL). The organic phases were combined and applied to a column charged with silica gel (1×10 cm), and the column was eluted with petroleum ether–ethyl acetate (1:3). The solvent was removed under reduced pressure, and the yields of **2a**–**5a** were determined by NMR. In run no. 7, compounds **2a**–**5a** were isolated by column chromatography on silica gel (gradient elution with petroleum ether–ethyl acetate, 10 to 80 vol % of the latter).

Heterogeneous peroxidation of triketones 1b–1f. The procedure was the same as described above in *b* (toluene, 20–25°C, 8 h). The organic phases were combined and applied to a column charged with silica gel (1×7 cm), and the column was eluted with 40 mL

of petroleum ether–ethyl acetate (1:3). The solvent was removed under reduced pressure, and the products were isolated by column chromatography on silica gel (gradient elution with petroleum ether–ethyl acetate, 10 to 80 vol % of the latter). The yields of **2b**–**5b** and **2c**–**5c** were almost the same when the catalyzed was recycled. The NMR spectra of **2**–**5** were identical to those given in [26].

1-[(1*R*,2*R*,5*S*)-2-Benzyl-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octan-2-yl]ethanone (2a). Yield 0.035 g (11%), colorless oily material, n_D^{22} = 1.5162 (1.5160 [26]). ^{1}H NMR spectrum, δ, ppm: 1.47 s (3H, 1-CH_3), 1.52–1.62 m (4H, 5-CH_3, 3-H), 1.75–1.85 m and 1.90–2.03 m (1H each, 4-H), 2.14 s (3H, CH_3C=O), 2.56–2.70 m (1H, 3-H), 2.88 d and 3.53 d (1H each, C**H**$_2$Ph, *J* = 13.2 Hz), 7.03–7.09 m (2H, H_{arom}), 7.15–7.26 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 18.4 (1-CH_3), 20.8 (5-CH_3), 22.3 (C^3), 30.3 (**C**H_3C=O), 31.0 (C^4), 36.2 (**C**H_2Ph), 59.2 (C), 109.2 (C^5), 111.4 (C^1); 126.6, 128.3, 130.2 (CH_{arom}); 137.7 (C_{arom}), 210.9 (C=O). Found, %: C 69.50; H 7.40. $C_{16}H_{20}O_4$. Calculated, %: C 69.54; H 7.30.

1-[(1*R*,2*S*,5*S*)-2-Benzyl-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octan-2-yl]ethanone (3a). Yield 0.029 g (9%), white crystals, mp 89–90°C (from EtOAc) [26]. ^{1}H NMR spectrum, δ, ppm: 1.50 s (3H, 5-CH_3), 1.61–1.78 m (4H, 1-CH_3, 3-H), 1.86–1.96 m (2H, 4-H), 2.07 s (3H, CH_3C=O), 2.18–2.34 m (1H, 3-H), 2.59 d and 3.35 d (1H each, C**H**$_2$Ph, *J* = 13.2 Hz), 7.00–7.10 m (2H, H_{arom}), 7.15–7.29 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 18.9 (1-CH_3), 20.6 (5-CH_3), 25.8 (C^3), 30.0 (**C**H_3C=O), 33.0 (C^4), 41.4 (**C**H_2Ph), 58.3 (C^2), 109.0 (C^5), 111.3 (C^1); 126.7, 128.3, 130.1 (CH_{arom}); 136.0 (C_{arom}), 210.3 (C=O). Found, %: C 69.45; H 7.35. $C_{16}H_{20}O_4$. Calculated, %: C 69.54; H 7.30.

1-[(1*R*,2*R*,5*S*)-1,5-Dimethyl-2-(4-nitrobenzyl)-6,7,8-trioxabicyclo[3.2.1]octan-2-yl]ethanone (2b). Yield 0.044 g (14%), white crystals, mp 115–116°C (from EtOAc) [26]. ^{1}H NMR spectrum, δ, ppm: 1.37–1.49 m (4H, 1-CH_3, 3-H), 1.58 s (3H, 5-CH_3), 1.77–2.03 m (2H, 4-H), 2.21 s (3H, CH_3C=O), 2.64–2.79 m (1H, 3-H), 3.00 d and 3.66 d (1H each, C**H**$_2C_6H_4$, *J* = 13.2 Hz), 7.27 d (2H, H_{arom}, *J* = 8.8 Hz), 8.08 d (2H, H_{arom}, *J* = 8.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.2 (1-CH_3), 20.7 (5-CH_3), 22.2 (C^3), 29.9 (**C**H_3C=O), 30.8 (C^4), 35.4 (2-CH_2), 59.6 (C^2), 109.2 (C^5), 110.8 (C^1), 123.4 and 131.2 (C^o, C^m), 145.8 (C^i), 146.8 (C^p), 210.3 (C=O). Found, %: C 59.74; H 5.82; N 4.40. $C_{16}H_{19}NO_6$. Calculated, %: C 59.81; H 5.96; N 4.36.

1-[(1*R*,2S,5*S*)-1,5-Dimethyl-2-(4-nitrobenzyl)-6,7,8-trioxabicyclo[3.2.1]octan-2-yl]ethanone (3b). Yield 0.038 g (12%), white crystals, mp 133–134°C (from EtOAc) [26]. ^{1}H NMR spectrum, δ, ppm: 1.48–1.61 m (4H, 5-CH_3, 3-H), 1.66 s (3H, 1-CH_3), 1.89–2.09 m (2H, 4-H), 2.13–2.31 m (4H, CH_3C=O, 3-H), 2.67 d and 3.54 d (1H each, 2-CH_2, *J* = 13.2 Hz), 7.25 d (2H, H_{arom}, *J* = 8.8 Hz), 8.09 d (2H, H_{arom}, *J* = 8.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.5 (1-CH_3), 20.6 (5-CH_3), 25.5 (C^3), 30.1 (**C**H_3C=O), 32.8 (C^4), 40.6 (2-CH_2), 58.3 (C^2), 109.0 (C^5), 110.6 (C^1), 123.3 and 131.1 (C^o, C^m), 144.3 (C^i), 147.0 (C^p), 209.5 (C=O). Found, %: C 59.90; H 5.90; N 4.38. $C_{16}H_{19}NO_6$. Calculated, %: C 59.81; H 5.96; N 4.36.

1-[(1*R*,2*R*,5*S*)-1,5-Dimethyl-2-(4-methylbenzyl)-6,7,8-trioxabicyclo[3.2.1]octan-2-yl]ethanone (2c). Yield 0.044 g (14%), yellow oily material, n_D^{22} = 1.5214 (1.5215 [26]). ^{1}H NMR spectrum, δ, ppm: 1.48 s (3H, 1-CH_3), 1.51–1.65 m (4H, 5-CH_3, 3-H), 1.74–1.86 m and 1.90–2.04 m (1H each, 4-H), 2.14 s (3H, CH_3C=O), 2.28 s (3H, C**H**$_3C_6H_4$), 2.55–2.71 m (1H, 3-H), 2.85 d and 3.49 d (1H, 2-CH_2, *J* = 13.2 Hz), 6.95 d (2H, H_{arom}, *J* = 8.1 Hz), 7.03 d (2H, H_{arom}, *J* = 8.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.4 (1-CH_3), 20.8 (5-CH_3), 20.9 (**C**$H_3C_6H_4$), 22.3 (C^3), 30.3 (**C**H_3C=O), 30.9 (C^4), 35.8 (2-CH_2), 59.1 (C^2), 109.2 (C^5), 111.4 (C^5), 129.0 and 130.0 (C^o, C^m), 134.5 (C^p), 136.1 (C^i), 211.0 (C=O). Found, %: C 70.30; H 7.68. $C_{17}H_{22}O_4$. Calculated, %: C 70.32; H 7.64.

1-[(1*R*,2*S*,5*S*)-1,5-Dimethyl-2-(4-methylbenzyl)-6,7,8-trioxabicyclo[3.2.1]octan-2-yl]ethanone (3c). Yield 0.032 g (10%), white crystals, mp 90–91°C (from EtOAc) [26]. ^{1}H NMR spectrum, δ, ppm: 1.50 s (3H, 5-CH_3), 1.62–1.78 m (4H, 1-CH_3, 3-H), 1.85–1.96 m (2H, 4-H), 2.07 m (3H, CH_3C=O), 2.13–2.35 m (4H, C**H**$_3C_6H_4$, 3-H), 2.56 d and 3.30 d (1H each, 2-CH_2, *J* = 13.2 Hz), 6.93 d (2H, H_{arom}, *J* = 8.1 Hz), 7.04 d (2H, H_{arom}, *J* = 8.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.9 (1-CH_3), 20.6 (5-CH_3), 21.0 (**C**$H_3C_6H_4$), 25.8 (C^3), 30.0 (**C**H_3C=O), 33.1 (C^4), 41.0 (2-CH_2), 58.3 (C^2), 109.0 (C^5), 111.3 (C^1), 128.9 and 130.0 (C^o, C^m), 132.8 (C^p), 136.3 (C^i), 210.4 (C=O). Found, %: C 70.40; H 7.70. $C_{17}H_{22}O_4$. Calculated, %: C 70.32, H 7.64.

1-[(1*R*,2*R*,5*S*)-2-(4-Chlorobenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octan-2-yl]ethanone (2d). Yield 0.060 g (19%), white crystals, mp 121–122°C (from EtOAc) [26]. ^{1}H NMR spectrum, δ, ppm: 1.44 s (3H, 1-CH_3), 1.48–1.62 m (4H, 5-CH_3, 3-H), 1.76–1.99 m (2H, 4-H), 2.17 s (3H, CH_3C=O), 2.59–2.73 m

(1H, 3-H), 2.85 d and 3.51 d (1H each, 2-CH_2, J = 13.6 Hz), 7.01 d (2H, H_{arom}, J = 8.4 Hz), 7.19 d (2H, H_{arom}, J = 8.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.3 (1-CH_3), 20.8 (5-CH_3), 22.2 (C^3), 30.2 (**C**H_3C=O), 30.9 (C^4), 35.2 (2-CH_2), 59.3 (C^2), 109.2 (C^5), 111.1 (C^1), 128.4 and 131.6 (C^o, C^m), 132.5 (C^p), 136.2 (C^i), 210.7 (C=O). Found, %: C 61.92; H 6.23; Cl 11.51. $C_{16}H_{19}ClO_4$. Calculated, %: C 61.84; H 6.16; Cl 11.41.

1-[(1*R*,2*S*,5*S*)-2-(4-Chlorobenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octan-2-yl]ethanone (3d). Yield 0.032 g (10%), white crystals, mp 105–106°C (from EtOAc) [26]. ^1H NMR spectrum, δ, ppm: 1.48–1.73 m (7H, 1-CH_3, 5-CH_3, 3-H), 1.87–2.01 m (2H, 4-H), 2.08–2.29 m (4H, CH_3C=O, 3-H), 2.54 d and 3.35 d (1H each, 2-CH_2, J = 12.9 Hz), 6.98 d (2H, H_{arom}, J = 8.3 Hz), 7.20 d (2H, H_{arom}, J = 8.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.7 (1-CH_3), 20.6 (5-CH_3), 25.6 (C^3), 30.1 (**C**H_3C=O), 32.9 (C^4), 40.5 (2-CH_2), 58.2 (C^2), 109.0 (C^5), 111.0 (C^1), 128.4 and 131.5 (C^o, C^m), 132.7 (C^p), 134.6 (C^i), 210.0 (C=O). Found, %: C 61.92; H 6.22; Cl 11.53. $C_{16}H_{19}ClO_4$. Calculated, %: C 61.84; H 6.16; Cl 11.41.

1-[(1*R*,2*R*,5*S*)-2-(4-Bromobenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octan-2-yl]ethanone (2e). Yield 0.035 g (11%), white crystals, mp 109–110°C [26]. ^1H NMR spectrum, δ, ppm: 1.35–1.63 m (7H, 1-CH_3, 5-CH_3, 3-H), 1.74–2.00 m (2H, 4-H), 2.18 s (3H, CH_3C=O), 2.57–2.75 m (1H, 3-H), 2.84 d and 3.50 d (1H each, 2-CH_2, J = 13.2 Hz), 6.96 d (2H, H_{arom}, J = 8.1 Hz), 7.35 d (2H, H_{arom}, J = 8.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.3 (1-CH_3), 20.8 (5-CH_3), 22.2 (C^3), 30.2 (**C**H_3C=O), 30.9 (C^4), 35.3 (2-CH_2), 59.2 (C^2), 109.2 (C^5), 111.1 (C^1), 120.6 (C^p), 131.4 and 132.0 (C^o, C^m), 136.8 (C^i), 210.7 (C=O). Found, %: C 54.05; H 5.46; Br 22.59. $C_{16}H_{19}BrO_4$. Calculated, %: C 54.10; H 5.39; Br 22.49.

1-[(1*R*,2*S*,5*S*)-2-(4-Bromobenzyl)-1,5-dimethyl-6,7,8-trioxabicyclo[3.2.1]octan-2-yl]ethanone (3e). Yield 0.028 g (8%), white crystals, mp 107–108°C [26]. ^1H NMR spectrum, δ, ppm: 1.46–1.72 m (7H, 1-CH_3, 5-CH_3, 3-H), 1.87–1.98 m (2H, 4-H), 2.11 s (3H, CH_3C=O), 2.13–2.28 m (1H, 3-H), 2.52 d and 3.33 d (1H each, 2-CH_2, J = 12.8 Hz), 6.93 d (2H, H_{arom}, J = 8.3 Hz), 7.35 d (2H, H_{arom}, J = 8.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.7 (1-CH_3), 20.6 (5-CH_3), 25.6 (C^3), 30.1 (**C**H_3C=O), 32.9 (C^4), 40.6 (2-CH_2), 58.1 (C^2), 109.0 (C^5), 111.0 (C^1), 120.8 (C^p), 131.4 and 131.9 (C^o, C^m), 135.2 (C^i), 210.0 (C=O). Found, %: C 54.15; H 5.45; Br 22.60. $C_{16}H_{19}BrO_4$. Calculated, %: C 54.10; H 5.39; Br 22.49.

3a-Benzyl-3,6,7a-trimethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran (4a). Yield 0.080 g (25%), white crystals, mp 94–95°C (from EtOAc) [26]. ^1H NMR spectrum, δ, ppm: 1.37 s (3H, 6-CH_3), 1.42 s (6H, 3-CH_3, 7a-CH_3), 1.64–1.77 m (2H, 5-H), 1.78–1.89 m (2H, 4-H), 2.86 s (2H, 3a-CH_2), 7.16–7.33 m (5H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 16.1 (3-CH_3, 7a-CH_3), 18.9 (C^4), 24.7 (6-CH_3), 30.9 (C^5), 36.8 (3a-CH_2), 51.8 (C^{3a}), 93.7 (C^6), 107.5 (C^3, C^{7a}); 126.8, 128.1, 131.2 (CH_{arom}); 136.5 (C^i). Found, %: C 69.47; H 7.32. $C_{16}H_{20}O_4$. Calculated, %: C 69.54; H 7.30.

3,6,7a-Trimethyl-3a-(4-nitrobenzyl)tetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran (4b). Yield 0.069 g (22%), white crystals, mp 149–150°C (from EtOAc) [26]. ^1H NMR spectrum, δ, ppm: 1.40 s (3H, 6-CH_3), 1.43 s (6H, 3-CH_3, 7a-CH_3), 1.69–1.80 m (2H, 5-H), 1.80–1.92 m (2H, 4-H), 2.98 s (2H, 3a-CH_2), 7.43 d (2H, H_{arom}, J = 8.8 Hz), 8.17 d (2H, H_{arom}, J = 8.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.7 (3-CH_3, 7a-CH_3), 19.0 (C^4), 24.6 (6-CH_3), 30.7 (C^5), 36.8 (3a-CH_2), 51.9 (C^{3a}), 93.8 (C^6), 107.2 (C^3, C^{7a}), 123.3 and 131.9 (C^o, C^m), 144.4 (C^i), 147.0 (C^p). Found, %: C 59.90; H 5.84; N 4.40. $C_{16}H_{19}NO_6$. Calculated, %: C 59.81; H 5.96; N 4.36.

3,6,7a-Trimethyl-3a-(4-methylbenzyl)tetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran (4c). Yield 0.063 g (20%), white crystals, mp 106–107°C (from EtOAc) [26]. ^1H NMR spectrum, δ, ppm: 1.38 s (3H, 6-CH_3), 1.42 s (6H, 3-CH_3, 7a-CH_3), 1.64–1.74 m (2H, 5-H), 1.76–1.88 m (2H, 4-H), 2.32 s (3H, C**H**$_3$C$_6$H$_4$), 2.82 s (2H, 3a-CH_2), 7.04–7.12 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 16.6 (3-CH_3, 7a-CH_3), 18.9 (C^4), 21.0 (**C**$H_3C_6H_4$), 24.7 (6-CH_3), 30.9 (C^5), 36.3 (3a-CH_2), 51.7 (C^{3a}), 93.7 (C^6), 107.5 (C^3, C^{7a}), 128.8 and 131.0 (C^o, C^m), 133.2 (C^p), 136.4 (C^i). Found, %: C 70.25; H 7.55. $C_{17}H_{22}O_4$. Calculated, %: C 70.32; H 7.64.

3a-(4-Chlorobenzyl)-3,6,7a-trimethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran (4d). Yield 0.079 g (25%), white crystals, mp 120–121°C (from EtOAc) [26]. ^1H NMR spectrum, δ, ppm: 1.32 s (3H, 6-CH_3), 1.35 s (6H, 3-CH_3, 7a-CH_3), 1.59–1.69 m (2H, 5-H), 1.69–1.80 m (2H, 4-H), 2.77 s (2H, 3a-CH_2), 7.09 d (2H, H_{arom}, J = 8.4 Hz), 7.19 d (2H, H_{arom}, J = 8.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.7 (3-CH_3, 7a-CH_3), 18.9 (C^4), 24.6 (6-CH_3), 30.8 (C^5), 36.2 (3a-CH_2), 51.7 (C^{3a}), 93.7 (C^6), 107.4 (C^3, C^{7a}), 128.3 and 132.4 (C^o, C^m), 132.9 (C^p), 134.9 (C^i). Found, %: C 61.80; H 6.21; Cl 11.53. $C_{16}H_{19}ClO_4$. Calculated, %: C 61.84; H 6.16; Cl 11.41.

3a-(4-Bromobenzyl)-3,6,7a-trimethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran (4e). Yield 0.079 g (25%), white crystals, mp 123–124°C (from EtOAc) [26]. ^{1}H NMR spectrum, δ, ppm: 1.38 s (3H, 6-CH_3), 1.41 s (6H, 3-CH_3, 7a-CH_3), 1.64–1.74 m (2H, 5-H), 1.75–1.86 m (2H, 4-H), 2.81 s (2H, 3a-CH_2), 7.09 d (2H, H_{arom}, J = 8.2 Hz), 7.40 d (2H, H_{arom}, J = 8.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.7 (3-CH_3, 7a-CH_3), 18.9 (C^4), 24.7 (6-CH_3), 30.8 (C^5), 36.3 (3a-CH_2), 51.6 (C^{3a}), 93.7 (C^6), 107.4 (C^3, C^{7a}), 120.9 (C^p), 131.3 and 132.8 (C^o, C^m), 135.4 (C^i). Found, %: C 54.05; H 5.45; Br 22.53. $C_{16}H_{19}BrO_4$. Calculated, %: C 54.10; H 5.39; Br 22.49.

4-(7-Benzyl-1,4-dimethyl-2,3,5,6-tetraoxabicyclo-[2.2.1]heptan-7-yl)butan-2-one (5a). Yield 0.081 g (24%), white crystals, mp 69–70°C (from EtOAc) [26]. ^{1}H NMR spectrum, δ, ppm: 1.22 s (6H, CH_3), 2.04–2.15 m (2H, 4′-H), 2.18 s (3H, CH_3C=O), 2.62–2.73 m (2H, 3′-H), 3.00 s (2H, 7-CH_2), 7.16–7.35 m (5H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 9.2 (CH_3), 21.5 ($C^{4'}$), 30.1 (**C**H_3C=O), 34.1 (7-CH_2), 38.1 ($C^{3'}$), 60.1 (C^7), 112.0 (C^1, C^4); 127.2, 128.4, 130.9 (CH_{arom}); 135.2 (C_{arom}), 206.9 (C=O). Found, %: C 65.68; H 7.02. $C_{16}H_{20}O_5$. Calculated, %: C 65.74; H 6.90.

4-[1,4-Dimethyl-7-(4-nitrobenzyl)-2,3,5,6-tetra-oxabicyclo[2.2.1]heptan-7-yl]butan-2-one (5b). Yield 0.083 g (25%), white crystals, mp 121–122°C (from EtOAc) [26]. ^{1}H NMR spectrum, δ, ppm: 1.22 s (6H, CH_3), 2.04–2.17 m (2H, 4′-H), 2.21 s (3H, CH_3C=O), 2.67–2.77 m (2H, 3′-H), 3.10 s (2H, 7-CH_2), 7.46 d (2H, H_{arom}, J = 8.1 Hz), 8.18 d (2H, H_{arom}, J = 8.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.3 (CH_3), 21.6 ($C^{4'}$), 30.2 (**C**H_3C=O), 34.3 (7-CH_2), 37.9 ($C^{3'}$), 60.2 (C^7), 111.8 (C^1, C^4), 123.6 and 131.9 (C^o, C^m), 143.1 (C^i), 147.3 (C^p), 206.6 (C=O). Found, %: C 56.87; H 5.60; N 4.25. $C_{16}H_{19}NO_7$. Calculated, %: C 56.97; H 5.68; N 4.15.

4-[1,4-Dimethyl-7-(4-methylbenzyl)-2,3,5,6-tetraoxabicyclo[2.2.1]heptan-7-yl]butan-2-one (5c). Yield 0.064 g (19%), light yellow crystals, mp 79–80°C (from EtOAc) [26]. ^{1}H NMR spectrum, δ, ppm: 1.23 s (6H, CH_3), 1.99–2.25 m (5H, CH_3C=O, 4′-H), 2.31 s (3H, C**H**$_3C_6H_4$), 2.61–2.74 m (2H, 3′-H), 2.96 s (2H, 7-CH_2), 7.04–7.17 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 9.3 (CH_3), 21.0 (**C**$H_3C_6H_4$), 21.5 ($C^{4'}$), 30.1 (**C**H_3C=O), 33.7 (7-CH_2), 38.1 ($C^{3'}$), 60.1 (C^7), 112.0 (C^1, C^4), 129.1 and 130.8 (C^o, C^m), 132.0 (C^p), 136.8 (C^i), 207.0 (C=O). Found, %: C 66.60; H 7.30. $C_{17}H_{22}O_5$. Calculated, %: C 66.65; H 7.24.

4-[7-(4-Chlorobenzyl)-1,4-dimethyl-2,3,5,6-tetra-oxabicyclo[2.2.1]heptan-7-yl]butan-2-one (5d). Yield 0.076 g (23%), white crystals, mp 96–97°C (from EtOAc) [26]. ^{1}H NMR spectrum, δ, ppm: 1.23 s (6H, CH_3), 2.01–2.13 m (2H, 4′-H), 2.19 s (3H, CH_3C=O), 2.64–2.73 m (2H, 3′-H), 2.97 s (2H, 7-CH_2), 7.19 d (2H, H_{arom}, J = 8.4 Hz), 7.28 d (2H, H_{arom}, J = 8.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.3 (CH_3), 21.6 ($C^{4'}$), 30.2 (**C**H_3C=O), 33.7 (7-CH_2), 38.1 ($C^{3'}$), 60.1 (C^7), 111.9 (C^1, C^4), 128.6 and 132.3 (C^o, C^m), 133.3 (C^p), 133.7 (C^i), 206.9 (C=O). Found, %: C 58.86; H 5.93; Cl 10.98. $C_{16}H_{19}ClO_5$. Calculated, %: C 58.81; H 5.86; Cl 10.85.

4-[7-(4-Bromobenzyl)-1,4-dimethyl-2,3,5,6-tetra-oxabicyclo[2.2.1]heptan-7-yl]butan-2-one (5e). Yield 0.066 g (20%), white crystals, mp 82–83°C (from EtOAc) [26]. ^{1}H NMR spectrum, δ, ppm: 1.23 s (6H, CH_3), 1.98–2.13 m (2H, 4′-H), 2.19 s (3H, CH_3C=O), 2.62–2.73 m (2H, 3′-H), 2.95 s (2H, 7-CH_2), 7.13 d (2H, H_{arom}, J = 8.4 Hz), 7.43 d (2H, H_{arom}, J = 8.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.3 (CH_3), 21.5 ($C^{4'}$), 30.2 (**C**H_3C=O), 33.8 (7-CH_2), 38.0 ($C^{3'}$), 60.0 (C^7), 111.9 (C^1, C^4), 121.3 (C^p), 131.6 and 132.6 (C^o, C^m), 134.2 (C^i), 206.9 (C=O). Found, %: C 51.85; H 5.29; Br 21.65. $C_{16}H_{19}BrO_5$. Calculated, %: C 51.77; H 5.16; Br 21.52.

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