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Photochemical rearrangement of 5,6-epoxy derivatives of the Diels–Alder adduct of levoglucosenone and piperylene

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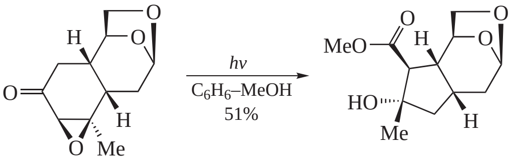
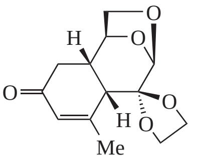
Photolysis of 5,6-epoxy 4-keto derivatives of the Diels–Alder adduct of levoglucosenone and piperylene in C_6H_6–MeOH causes cleavage of the C^4–C^5 bond giving product containing vicinal acetone and alkyl acetate moieties, the latter would further transform into 1-alkoxycarbonyl-2-hydroxy-2-methylcyclopentane derivative annulated to 5,8-dioxabicyclo[3.2.1]-octane cage.



Development of methods for constriction of cyclohexene fragment in the Diels–Alder adducts of levoglucosenone and 1,3-dienes is perspective for the preparation of chiral subunits for iridoids.[1] Heterolytic rupture of various functionalized cyclohexenes followed by their transformation into cyclopentane derivatives has been studied.[2] Previous examples of such a transformation relate to steroids[3] and a trivial 4,4-dimethyl-2-cyclohexenone.[4] In case of keto epoxides, the reaction proceeds more efficiently.[5] 3,4-Epoxy olefins on photoirradiation in acetone are converted into β,γ-unsaturated ketones.[6] However, similar photochemical constriction of cyclohexene moiety in the Diels–Alder levoglucosenone and 1,3-diene adducts has not been so far reported. Therefore, we herein studied the photolysis of derivatives of these Diels–Alder adducts, namely, enone **1**, keto epoxide **2**, and its analogue **3**[2] lacking spiro-fused ethylenedioxy fragment.



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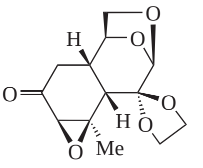

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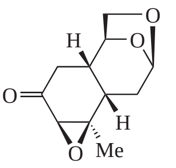

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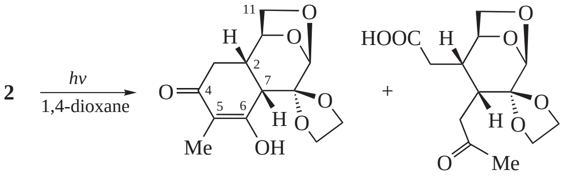
Attempted photolysis of compounds **1** and **2** in C_6H_6, CH_2Cl_2, MeOH, acetone–THF and MeOH–THF[7] afforded mixtures of products which we failed to separate and identify. However, photoirradiation of keto oxirane **2** in 1,4-dioxane gave two products, keto enol **4** and keto acid **5**,[†] whose formation occurred analogously to the literature[5] (Scheme 1).

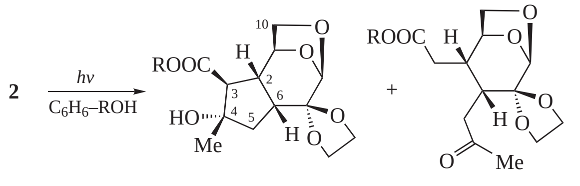


4, 46% **5**, 30%

Scheme 1

Enone system in the ^{13}C NMR spectra of compound **4** gives resonance at 109.31 (C^5), 173.59 (C^6) and at 207.79 ppm (C=O). According to correlations in COSY and HMBC experiments, this carbonyl carbon atom is located in the 4-position. Proton H^7 resonates as doublet at 3.33 ppm with $^3J_{H(7)\text{-}H(2)}$ 7.2 Hz, which indicates *syn*-arrangement of H^2 and H^7, the presence of the correlation peaks H^{11A}/H^2 and H^{11A}/H^7 in the NOESY spectra is the result of *S*-configuration of centres C^2 and C^7.

Carrying out the reaction in benzene containing 1% methanol (see ref. 7) afforded cyclopentane annulated derivative **6a** along with keto ester **7a**, a product of cyclohexane ring opening[‡] (Scheme 2).



6a R = Me, 37% **7a** R = Me, 19%
6b R = Pr^i, 12% **7b** R = Pr^i, 21%

Scheme 2

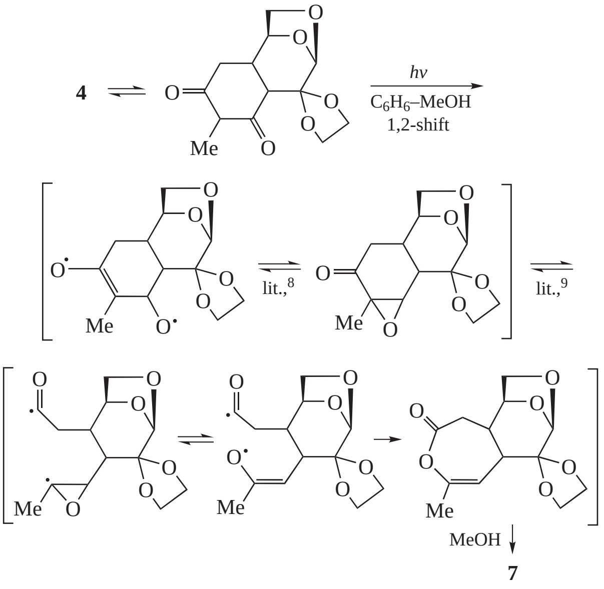
[†] *(1*S*,2*S*,7*S*,9*R*)-6-Hydroxy-5-methyl-4*H*-spiro[10,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-5-ene-8,2'-[1,3]dioxolan]-4-one* **4** *and {(1'*R*,3'*R*,4'*S*,5'*S*)-3'-(2-oxopropyl)spiro[7,8-dioxabicyclo[3.2.1]octane-2,2-[1,3]dioxolan]-4-yl}acetic acid* **5**. A solution of keto epoxide **2** (0.08 g, 0.03 mmol) in 1,4-dioxane (4 ml) and H_2O (0.04 ml) was irradiated at room temperature until the reaction was complete (~18 h). The solvent was distilled off under reduced pressure, and the residue was purified by chromatography on silica gel. Yields: **4**, 0.04 g (46%); **5**, 0.03 g (30%).

[‡] *Methyl (1*S*,2*R*,3*R*,4*S*,6*S*,8*R*)-4-hydroxy-4-methylspiro[9,11-dioxatricyclo[6.2.1.0^{2,6}]undecane-7,2'[1,3]dioxolane]-3-carboxylate* **6a** *and methyl {(1'*R*,3'*R*,4'*S*,5'*S*)-3'-(2-oxopropyl)spiro[7,8-dioxabicyclo[3.2.1]-octane-2,2'[1,3]dioxolan]-4'-yl}acetate* **7a**. A solution of epoxide **2** (0.11 g, 0.04 mmol) in anhydrous C_6H_6 (84 ml) and MeOH (0.84 ml) was purged with argon for 10 min and irradiated at room temperature until the reaction was complete (~18 h). The solvent was distilled off under reduced pressure, and the residue was purified by chromatography on silica gel. Yields: **6a**, 0.04 g (37%); **7a**, 0.02 g (19%).

Lowering the methanol content to 0.5% results in process deceleration and appearance of keto enol **4**. Switching from methanol to isopropanol leads to formation of the corresponding isopropyl esters **6b** and **7b**. These facts along with the published data[5] allow one to suppose that keto enol **4** is an intermediate on the way to cyclopentane derivatives **6** and fragmentation products **5** and **7**. Indeed, irradiation of keto enol **4** in benzene with 1% methanol gives compounds **6a** and **7a**.

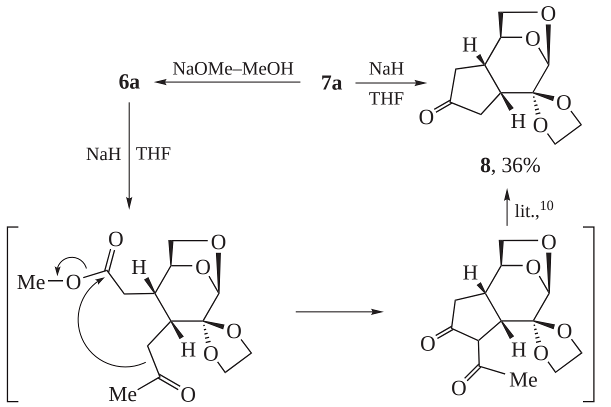
The presence of alcohol function in compound **6a** is confirmed by the signal at 80.03 ppm in ^{13}C NMR spectrum, which belongs to C^4 quaternary carbon correlating with protons at C^3, C^5 and the methyl group in the HMBC experiment. The ester carbon (171.89 ppm) in the HMBC experiment gives cross-peaks with protons at C^3, C^2 and with methoxy group. Correlations H^{10B}/H^2, H^{10B}/H^6, H^6/H^3 and H^2/Me in the NOESY spectra result from *R*-configured C^3 centre and *S*-configured C^4 and C^6 centres.

Methyl ketones **5**, **7a**, **7b** can be presumably formed as a result of C^4–C^5 bond rupture (Scheme 3). The alternative cleavage of C^5–C^6 bond is less likely since the oxygen atom at C^6 is more electron-deficient and tends to form hydrogen bonds with the dioxolane group.



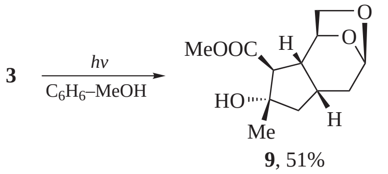
Scheme 3

The formation of cyclopentane derivative **6** can occur from methyl ketones **5**, **7** by intramolecular aldol-type reaction. In a control experiment, treatment of keto ester **7a** with NaH led to a complex mixture, from which cyclopentanone annulated derivative **8** was isolated in 36% yield.‡ On the other hand, carrying out the reaction under milder conditions (MeONa–MeOH) afforded cyclopentane derivative **6a** in 28% yield. Boiling compound **6a** in THF in the presence of NaH brought about cyclopentanone derivative **8** (Scheme 4). This transformation probably proceeds through stages of retro-Claisen condensation, intramolecular aldol-type condensation, and retro-Claisen deacetylation.[10]



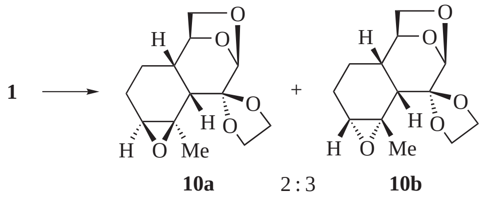
Scheme 4

Photolysis of compound **3** proceeds more efficiently in C_6H_6–MeOH (1%) affording thus cyclopentanone derivative **9** in 51% yield (Scheme 5).



Scheme 5

As expected, deoxo epoxy derivatives **10a**,**b** (available[2(*d*)] from enone **1**, Scheme 6) were resistant towards photolysis, in contrast to the published data.[11]



Scheme 6

In conclusion, photolysis of 5,6-epoxy ketones **2** and **3** gives products of constriction of the cyclohexane ring, cyclopentane derivatives **6**, **8** and **9**. The compounds herein obtained can be of interest to organic and medicinal chemists.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2017.05.006.

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§ *(1*S*,2*R*,6*R*,8*R*)-4*H*-Spiro[9,11-dioxatricyclo[6.2.1.0^{2,6}]undecane-7,2'-[1,3]dioxolan]-4-one* **8**. To a solution of ester **7a** (0.11 g, 0.38 mmol) in THF (5 ml) under an argon atmosphere, sodium hydride (0.04 g, 1.52 mmol) was added, and the mixture was refluxed until the initial compound was consumed (TLC monitoring). The mixture was treated with saturated aqueous solution of NH_4Cl, the products were extracted with EtOAc (2×4.0 ml). The combined extracts were dried with $MgSO_4$, evaporated, and the residue was chromatographed on silica gel. Yield 0.03 g (36%), white crystals, mp 125 °C. $[\alpha]_D^{20}$ +17 (*c* 0.26, CH_2Cl_2), R_f 0.2 (EtOAc–light petroleum, 1:1).

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