ISSN 1070-4280, Russian Journal of Organic Chemistry, 2008, Vol. 44, No. 6, pp. 814–822. © Pleiades Publishing, Ltd., 2008.
Published in Russian in Zhurnal Organicheskoi Khimii, 2008, Vol. 44, No. 6, pp. 825–833.

Oxidation Studies on Some Natural Monoterpenes: Citral, Pulegone, and Camphene*

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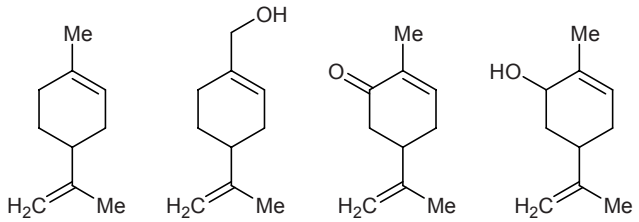
Received September 30, 2006

Abstract—Citral extracted from *Cymbopogon citratus* (*Gramineae*) was subjected to photochemical epoxidation with hydrogen peroxide to obtain a mixture of epoxy derivatives at the C^2=C^3 and C^6=C^7 double bonds. The thermal oxidation of citral with *m*-chloroperoxybenzoic acid at room temperature gave only the corresponding 6,7-epoxy derivative as a mixture of *E* and *Z* isomers with respect to the C^2=C^3 double bond. Photosensitized oxygenation of citral in the presence of tetraphenylporphyrin, Rose Bengal, or chlorophyll lead to a mixture of two isomeric hydroperoxides, (2*E*)-6-hydroperoxy-3,7-dimethylocta-2,7-dienal and (2*E*,5*E*)-7-hydroperoxy-3,7-dimethylocta-2,5-dienal. Epoxidation of pulegone isolated from *Penny royal* oil (*Mentha pulegium, Lamiaceae*) with hydrogen peroxide under irradiation with a sodium lamp lead to a mixture of *cis*- and *trans*-isomeric 2,2,6-trimethyl-1-oxaspiro[2.5]octan-4-ones, whereas under conditions of photosensitized oxygenation two hydroperoxide derivatives, 2-(1-hydroperoxy-1-methylethyl)-5-methylcyclohex-2-en-1-one and 2-hydroperoxy-5-methyl-2-(1-methylethenyl)cyclohexan-1-one, were also formed. Camphene reacted with hydrogen peroxide under irradiation to give a mixture of the corresponding *endo*- and *exo*-epoxy derivatives and camphor, while its thermal oxidation with *m*-chloroperoxybenzoic produced only the two former.

DOI: 10.1134/S1070428008060067

Natural monoterpenes, citral (**I**), pulegone (**II**), and camphene (**III**) were found in a wide variety of plants [1]; these compounds are non-nutrient dietary components of fruits and essential oils of citrus fruits, cherries, spearmint dill, caraway, apricots, and grapes. The most investigated monoterpenes are limonene, carvone, carveol, and perillyl alcohol, especially from the viewpoint of their chemotherapeutic activity [2].



A number of dietary monoterpenes were shown to act effectively in chemoprevention and chemotherapy of different cancers in animal models, at cellular level, and in human clinical trials [3–5]. On the other hand, plant monoterpenes are subjected to oxidation on exposure to air. Oxidation is enhanced by heat [6], irradiation [7], or chemical catalysts [8]. The oxidation process can also be initiated by attack of reactive singlet oxygen, as in photooxidation. Photooxidation provides an important way to produce hydroperoxides in the presence of oxygen, light energy, and photosensitizers [9]. Photosensitizers absorb visible or near-UV light to become electronically excited. Sensitizer in the triplet state reacts with oxygen through energy transfer to give singlet oxygen ($^1O_2$); the latter is highly electrophilic, and it reacts rapidly with double bonds of monoterpenes according to the ene mechanism. As a result, unstable neutral primary oxidation products such as hydroperoxides are formed. Hydroperoxides may give rise to secondary oxidation products having multiple chemical functional groups (hydroxy, oxo, and epoxy derivatives) [10]. Furthermore, unsaturated terpenes are capable of trapping activated oxygen species *in vivo* to give intermediate epoxides and hydroperoxides, which can alkylate or damage DNAs, proteins, and other biomolecules [6, 11].

It is well known that some monoterpenes undergo oxidation by the action of hydrogen peroxide under thermal conditions to give the corresponding epoxy

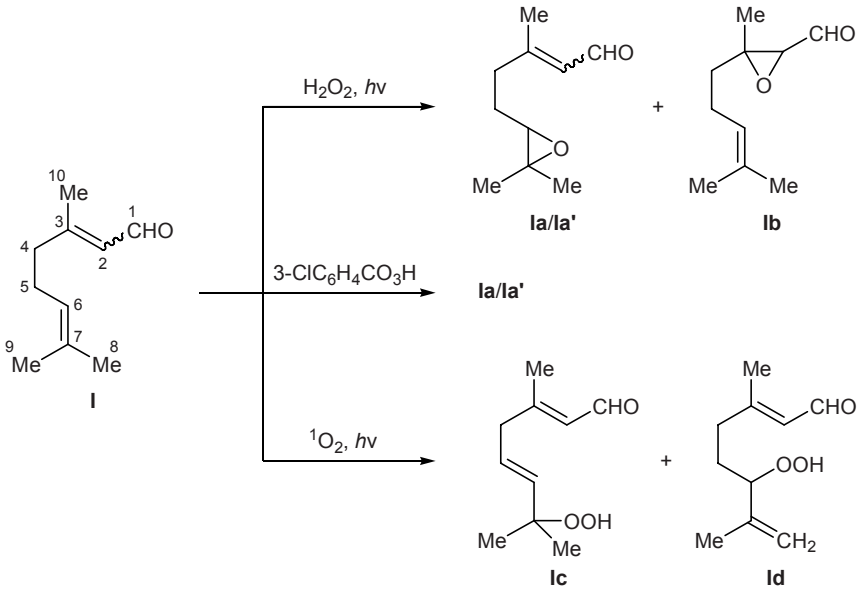
* The text was submitted by the authors in English.

derivatives [12, 13]; however, no attention was given to the preparation of such epoxides via photochemical oxidation reactions. Taking into account therapeutic importance of monoterpene compounds, we believed it to be relevant to examine some oxidation reactions of citral (**I**), pulegone (**II**), and camphene (**III**).

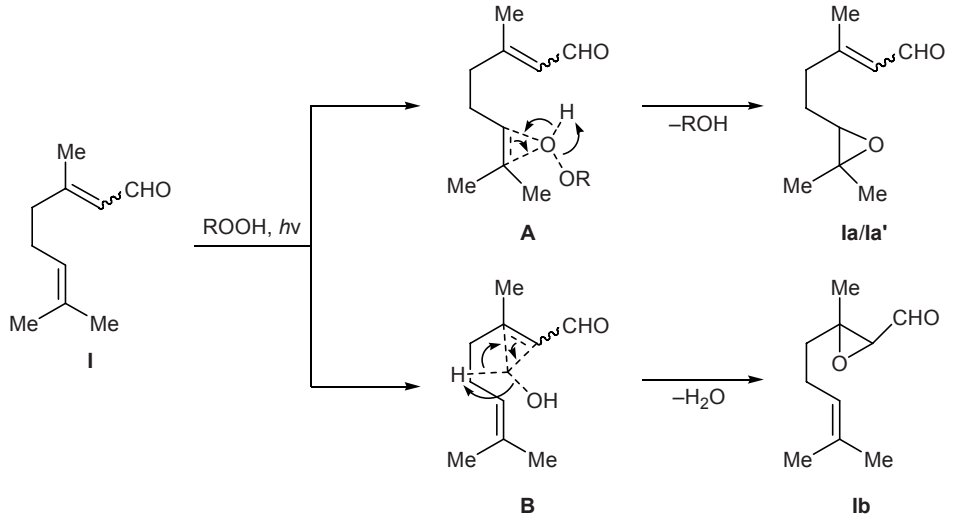
Citral [**I**, (2*E*,*Z*)-3,7-dimethylocta-2,6-dienal] is a monoterpene aldehyde which is the major component of *lemon grass oil* extracted from *Cymbopogon citratus* belonging to *Gramineae* [14–16] as a mixture of (2*E*)- and (2*Z*)-isomers at a ratio of 3:2 respectively. The ^{1}H NMR spectrum of (**I**) contains two doublets at δ 9.98 and 9.87 ppm with an intensity ratio of 3:2 from the aldehyde proton in the *E* and *Z* isomer, respectively. Photochemical epoxidation of citral (**I**) with 30% hydrogen peroxide in ethanol using a sodium lamp gave a mixture of (2*E*,*Z*)-5-(3,3-dimethyloxiran-2-yl)-3-methylpent-2-enal (**Ia**/**Ia′**) and 3-methyl-3-[(3*E*)-4-methylpent-3-en-1-yl)oxirane-2-carbaldehyde (**Ib**) in 21.5 and 11.5% yield, respectively (Scheme 1). The structure of compounds **Ia**/**Ia′** and **Ib** was determined on the basis of spectral measurements. The ^{1}H–^{1}H COSY spectrum of **Ia**/**Ia′** showed two upfield singlets at δ 1.27 and 1.32 ppm due to methyl groups on the oxirane ring, and a multiplet at δ 2.30 ppm from the methylene protons in position *4*; doublets at δ 5.85 and 9.97 ppm were assigned to the olefinic proton in position *2* and aldehyde proton, respectively, of the *Z* isomer (**Ia′**), while multiplet signal at δ 5.93 ppm and doublet at δ 9.99 ppm were attributed to the corresponding protons in the *E* isomer (**Ia**), the intensity ratio of the signals at δ 5.85 and 5.93 ppm being 36:64. Isomers **Ia** and **Ia′** were characterized by different retention times, 18.231 and 18.183 min, respectively (62 and 38%), and by the same *m*/*z* value (168) for the molecular ion (GC–MS data). Compound **Ib** displayed in the ^{1}H NMR spectrum singlets at δ 1.62 and 1.70 ppm from protons in the two methyl groups at the double bond and a doublet at δ 10.0 ppm from the aldehyde proton. The molecular ion of **Ib** had an *m*/*z* value of 168.

By oxidation of citral (**I**) with *m*-choroperoxybenzoic acid in chloroform at room temperature we obtained a mixture of *E*- and *Z*-epoxides **Ia** and **Ia′** at a ratio of 60:40 in an overall yield of about 60%, while no other products were detected (Scheme 1). Interestingly, the photooxygenation of compound **I** in the presence of tetraphenylporphyrin (TPP), Rose Bengal (RB), or chlorophyll (CP) as singlet oxygen sensitizer gave a mixture of (2*E*,5*E*)-7-hydroperoxy-3,7-dimethylocta-2,5-dienal (**Ic**) and (2*E*)-6-hydroperoxy-3,7-dimethylocta-2,7-dienal (**Id**) (Scheme 1) in an overall yield of 25.5, 11.5, and 15.6%, respectively, the ratio **Ic**:**Id** being 60:40 in all cases (according to the ^{1}H NMR data). The yield depended on the sensitizer activity, and it decreased in going from TPP to CP and then to RB. We succeeded in isolating by column chromatography only the major component, hydroperoxide **Ic**, as individual substance. The structure of products **Ic** and **Id** was confirmed by spectral data. Hydroperoxide **Ic** displayed in the ^{1}H–^{1}H NMR COSY spectrum a multiplet at δ 5.65 ppm and a dou-

Scheme 1.



Scheme 2.



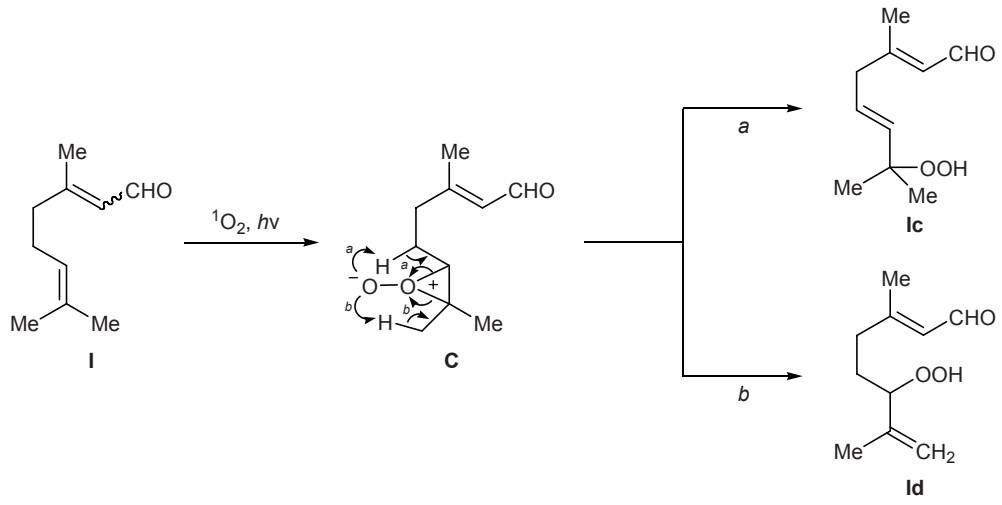
R = H, 3-ClC_6H_4CO.

blet at 5.72 ppm from the olefinic protons in positions *5* and *6*, respectively, and a singlet at δ 8.10 from the OOH proton. The ^{1}H NMR spectrum of **Id** contained a broadened singlet at δ 4.93 ppm from the 6-H proton and a singlet at δ 8.05 from the OOH proton. Compounds **Ic** and **Id** showed in the mass spectra the molecular ion peak with *m*/*z* 184.

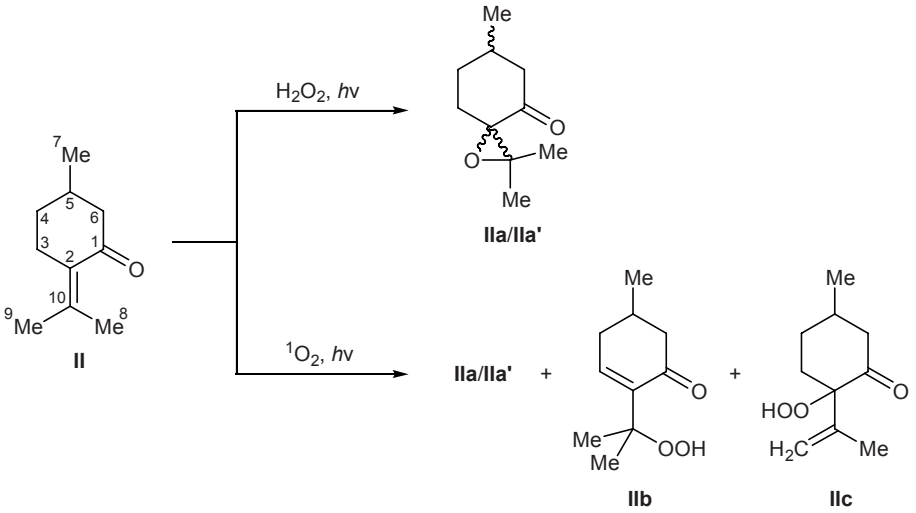
It is believed that citral (**I**) is oxidized with H_2O_2 in a thermal reaction. This behavior was studied previously by Yarovaya et al. [12] who reported that the epoxidation of **I** with hydrogen peroxide in acidic medium gave compounds **Ia** and **Ia′** and that in basic medium only epoxide **Ib** was formed as a mixture of *cis* and *trans* isomers. A probable mechanism for the formation of epoxy derivatives **Ia**, **Ia′**, and **Ib** is believed to involve oxirane intermediates **A** and **B**; elimination of water or *m*-chlorobenzoic acid molecule, depending on the oxidant used, gives the final products (Scheme 2). In the photosensitized oxidation of citral (**I**), hydroperoxides **Ic** and **Id** are likely to be formed through peroxirane intermediate **C** which is stabilized along two possible pathways *a* and *b* (Scheme 3).

Analogous oxidation reactions were performed with another natural monoterpene, pulegone (**II**, 2-isopropylidene-5-methylcyclohexan-1-one) which is the major component of *Penny royal oil*. Compound **II** was isolated by extraction of *Mentha pulegium* (*Lamiaceae*) leaves [17–20]. In the ^{1}H NMR spectrum of **II**, a doublet at δ 1.01 ppm due to 5-CH_3 group and two singlets at δ 1.78 and 1.98 ppm due to isopropylidene group were present. Photochemical epoxidation of pulegone (**II**) with 30% hydrogen peroxide in ethanol

Scheme 3.



Scheme 4.



under irradiation with a sodium lamp gave a mixture of 2,2,6-trimethyl-1-oxaspiro[2.5]octan-4-ones **IIa** and **IIa′** with different mutual orientations of the oxirane ring and 7-methyl group with respect to the cyclohexane ring; the overall yield of **IIa**/**IIa′** was about 40%, and their ratio was 45 : 55 (Scheme 4). The ^{1}H NMR spectrum contained doublets at δ 1.06 ppm (J = 7 Hz) from the axial methyl group on C^7 (α-isomer **IIa**) and at δ 1.09 ppm (J = 6 Hz) from the equatorial 7-methyl group (β-epoxide **IIa′**). Also, two singlets at δ 1.22 and 1.23 ppm were observed due to methyl groups on C^{10} in isomers **IIa** and **IIa′**, respectively. According to the GC–MS data, the molecular ions of **IIa** and **IIa′** have an m/z value of 168, and their retention times are 10.85 and 11.05 min, respectively (GC peak area ratio 45 : 55).

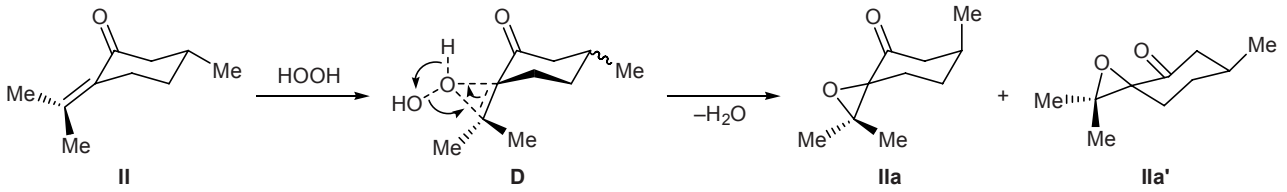
Photosensitized reaction of **II** with singlet oxygen in the presence of tetraphenylporphyrin (TPP), Rose Bengal (RB), and chlorophyll (CP) resulted in the formation of the above epoxides **IIa** and **IIa′**, 2-(1-hydroperoxy-1-methylethyl)-5-methylcyclohex-2-en-1-one (**IIb**), and 2-hydroperoxy-2-isopropenyl-5-methylcyclohexan-1-one (**IIc**). Compounds **IIb** and **IIc** were isolated as individual substances; the yields are given in table (Scheme 4). The structure of **IIb** and **IIc** was confirmed by spectral data. The ^{1}H NMR spectrum of **IIb** contained two singlets at δ 1.38 and 1.46 ppm from the side-chain isopropyl fragment, a doublet of doublets at δ 5.51 ppm (J = 3, 3.6 Hz) from the olefinic proton in position *3* of the cyclohexene ring, and a singlet at 8.8 ppm from the OOH group. Compound **IIb** was characterized by a retention time of 16.626 min (GC–MS), and its mass spectrum contained the molecular ion peak with m/z 184. Hydroperoxide **IIc** displayed in the ^{1}H NMR spectrum a doublet at δ 1.0 ppm and a singlet at δ 1.8 ppm from the C^7H_3 and C^8H_3 methyl groups, and the hydroperoxide proton resonated as a singlet at δ 9.85 ppm. The retention time

Photosensitized oxygenation of citral (**I**) and pulegone (**II**) in the presence of tetraphenylporphyrin, Rose Bengal, and chlorophyll

Initial comp. no.	Solvent	Sensitizer[a]	Reaction time, h	Overall yield, %	Products (ratio[b])
I	$CHCl_3$	TPP	7	25.5	**Ic**, **Id** (60 : 40)
I	EtOH	RB	7.5	11.5	**Ic**, **Id** (60 : 40)
I	$CHCl_3$	CP	7	15.6	**Ic**, **Id** (60 : 40)
II	$CHCl_3$	TPP	5.5	50	**IIa**/**IIa′**, **IIb**, **IIc** (30 : 38.5 : 31.5)
II	EtOH	RB	8	33	**IIa**/**IIa′**, **IIb**, **IIc** (18 : 45 : 37)
II	$CHCl_3$	CP	7	40	**IIa**/**IIa′**, **IIb**, **IIc** (25 : 41 : 34)

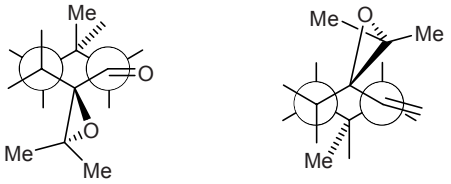
[a] TPP stands for tetraphenylporphyrin, RB stands for Rose Bengal, and CP stands for chlorophyll.
[b] The product ratios were calculated from the ^{1}H NMR spectrum of the reaction mixture.

Scheme 5.



of **IIc** was 19.053 min (GC–MS), and its molecular ion had the same *m*/*z* value as that of **IIb**.

Ngo et. al. [21] successfully prepared α- and β-epoxides **IIa** and **IIa′** at a ratio of 1:1 by oxidation of pulegone (**II**) with *m*-chloroperoxybenzoic acid at room temperature. A probable mechanism of formation of compounds **IIa** and **IIa′** is shown in Scheme 5. Addition of H_2O_2 at the exocyclic double bond can occur at both sides with respect to the cyclohexane ring; intermediate oxirane then loses H_2O molecule to give two isomeric products. The methyl group on C^7 and the oxirane oxygen atom are arranged *trans* with respect to each other in isomer **IIa** and *cis* in **IIa′**.



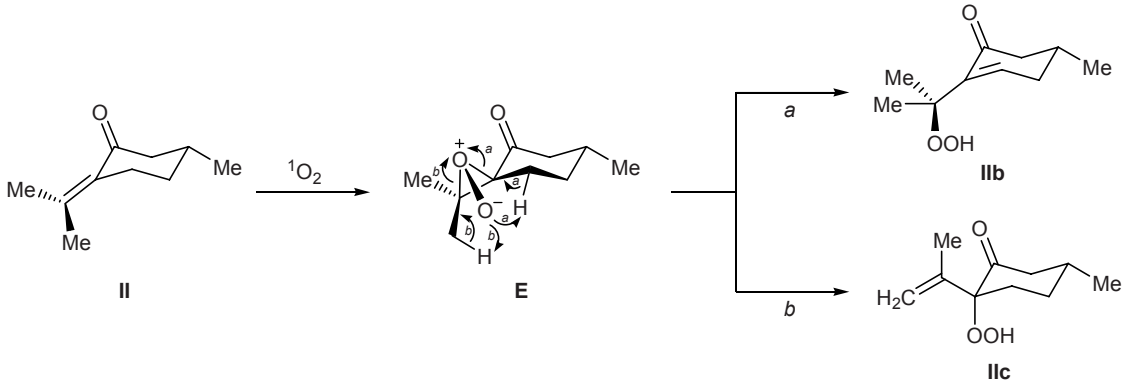
Photosensitized oxygenation of pulegone (**II**) is likely to involve peroxirane transition state **D** which is stabilized according to pathway *a* or *b*, yielding 2-(1-hydroperoxy-1-methylethyl)-5-methylcyclohex-2-en-1-one (**IIb**) and 2-hydroperoxy-2-isopropenyl-5-methylcyclohexan-1-one (**IIc**), respectively (Scheme 6), together with *cis*- and *trans*-epoxides **IIa′** and **IIa**.

We also performed epoxidation of camphene (**III**) under analogous conditions (30% hydrogen peroxide, ethanol, sodium lamp) and obtained a mixture of *endo*- and *exo*-isomers of 3,3-dimethylspiro[bicyclo[2.2.1]-heptane-2,2′-oxirane] (**IIIa**/**IIIa′**) in ~25% yield (ratio 2:1) and camphor (**IIIb**) in ~15% yield (Scheme 7). The oxidation of **III** with *m*-chloroperoxybenzoic acid in chloroform at room temperature gave 75% of epoxides **IIIa**/**IIIa′** (Scheme 7). Methylene protons in the oxirane ring **IIIa**/**IIIa′** appeared in the ^{1}H NMR spectrum of the isomer mixture as two doublets for each isomer at δ 2.67/2.69 (**IIIa**) and 2.75/2.78 ppm (**IIIa′**). The molecular ions of **IIIa**/**IIIa′** had an *m*/*z* value of 152. The ^{1}H NMR spectrum of **IIIb** was consistent with the spectrum of an authentic sample of camphor, which showed the absence of exocyclic methylene protons. The IR spectrum of **IIIb** contained a carbonyl absorption band at 1704 cm^{-1}.

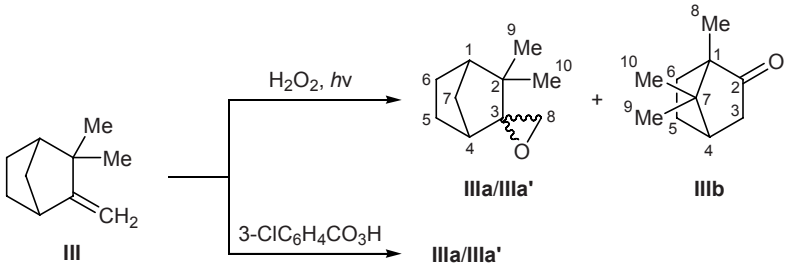
The formation of camphor **(IIIb)** in the photochemical epoxidation of camphene (**III**) with hydrogen peroxide seems to be unusual. Presumably, compound **IIIb** arises from photoinitiated rearrangement of **III**, followed by hydrogen peroxide attack as shown in (Scheme 8). Yarovaya et al [13] reported that epoxidation of **III** with hydrogen peroxide under thermal conditions gave epoxy derivatives **IIIa** and **IIIa′** at a ratio of 2.3:1. We have found no published data on photochemical epoxidation of camphene (**III**).

It is known that some hydroperoxides cause photochemical DNA damage [22, 23]. Therefore, compounds **Ic** and **IIb** were tested for DNA-damaging activity. For this purpose, a sample of DNA in saline was

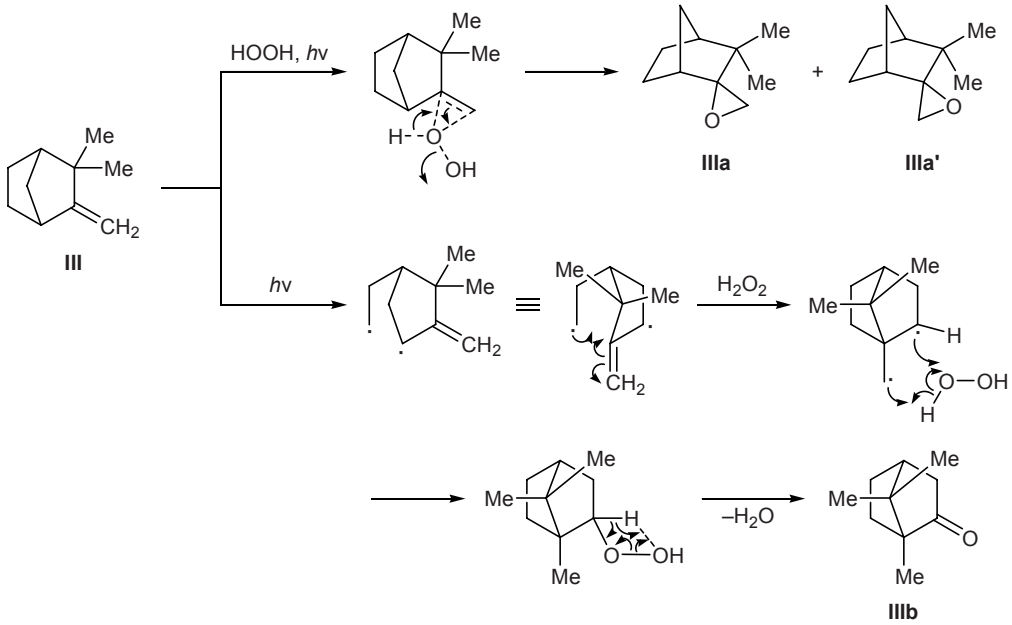
Scheme 6.



Scheme 7.



Scheme 8.



mixed with a solution of hydroperoxide **Ic** or **IIb** in ethanol, and the mixture was irradiated using a sodium lamp. The results (see Experimental) clearly indicated moderate and high degrees of DNA degradation in the presence of compounds **Ic** and **IIb**, respectively, when the irradiation time was prolonged to 8 h.

EXPERIMENTAL

Citral (**I**) and pulegone (**II**) were isolated by extraction of *Cymbopogon citratus* and *Manthu pulegium* plants, respectively, which were collected from Maddinah city (Saudi Arabia). Camphene (**III**) was supplied by Sigma Chemical Co. The melting points (uncorrected) were determined on a Fisher electric melting point apparatus. The IR spectra were recorded on a Perkin–Elmer 16 FPC FT-IR spectrophotometer from thin films (neat). The NMR spectra were measured from solutions in $CDCl_3$ on a Bruker Avance DPX 400 instrument (400 MHz for ^1H). Gas chromatography–mass spectrometry was performed using a Joel JMS 600H mass spectrometer coupled with a Hewlett–Packard HP 6890 Series gas chromatograph (HP-5 capillary column, 30 m×0.32 mm×0.25 μm; cross linked 5% dimethylpolysiloxane). A Philips G/5812 SON sodium lamp was used as irradiation source in photoinitiated reactions. Thin-layer chromatography (TLC) and preparative thin-layer chromatography were performed using Polygram SIL G/W 254 silica gel (Mecherey-Nagel). Solvents were removed from reaction mixtures and extracts using a rotary evaporator (20°C, 15 mm).

Citral [I, (2*E*,*Z*)-3,7-dimethylocta-2,6-dienal]. Colorless oil, $C_{10}H_{16}O$ (*M* 152.238). IR spectrum, ν, cm^{-1}: 2971, 2924, 1675, 1636, 1122. ^1H NMR spectrum, δ, ppm: *E* isomer: 1.58 s (3H, C^9H_3), 1.67 s (3H, C^8H_3), 2.17 s (3H, $C^{10}H_3$), 2.23 m (2H, 5-H), 2.59 d.d (2H, 4-H, *J* = 8 Hz), 5.08 m (1H, 6-H), 5.86 d (1H, 2-H, *J* = 8 Hz), 9.98 d (1H, CHO, *J* = 8 Hz); *Z* isomer: 1.99 s (3H, $C^{10}H_3$), 9.87 d (1H, CHO, *J* = 8 Hz); the other signals are the same as for the *E* isomer. ^{13}C NMR spectrum, δ_C, ppm: *E* isomer: 17.65 (C^9),

25.71 (C^{10}), 27.01 (C^5), 32.55 (C^8), 40.58 (C^4), 127.38 (C^6), 128.62 (C^2), 132.87 (C^7), 133.65 (C^3), 163.88 (C^1); *Z* isomer: 25 (C^{10}), 122.55 (C^2), 163.85 (C^1); the other signals are the same as for the *E* isomer.

Pulegone (II, 2-isopropylidene-5-methylcyclohexan-1-one). Colorless oil, $C_{10}H_{16}O$ (*M* 152.238). IR spectrum, ν, cm^{-1}: 2922, 1677, 1613, 1445, 1122. ^1H NMR spectrum, δ, ppm: 1.01 d (3H, C^7H_3, *J* = 7 Hz) 1.34 m (2H, 4-H), 1.78 s (3H, C^8H_3), 1.87 m (1H, 5-H), 1.98 s (3H, C^9H_3), 2.02 t (1H, 3-H), 2.26 t (1H, 3-H), 2.50 d.d (1H, 6-H, *J* = 16, 2 Hz), 2.72 d.d (1H, 6-H, *J* = 16, 5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 21.5 (C^8), 22 (C^9), 23 (C^7), 28.5 (C^3), 31.5 (C^5), 33 (C^4), 51 (C^6), 132 (C^{10}), 142 (C^2), 200 (C^1).

Photochemical epoxidation of natural terpenes I–III with hydrogen peroxide (*general procedure*). A 30% solution of hydrogen peroxide, 2.5 ml, was carefully added dropwise over a period of 5 min to a solution of 5 mmol of compound **I**–**III** in 25 ml of ethanol under stirring at 0°C. The mixture was irradiated with a sodium lamp for 55 h (in the reactions with **I** and **II**) or 21 h (in the reaction with **III**) under nitrogen. The mixture was then evaporated under reduced pressure at room temperature, the gummy residue was treated with 25 ml of chloroform, and the extract was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel using petroleum ether (bp 60–80°C)–diethyl ether (9:2) as eluent to isolate: from **I**: 0.18 g of isomer mixture **Ia**/**Ia′** and 0.10 g of compound **Ib**, ratio **Ia**/**Ia′**:**Ib** = 64:36, overall yield 33%; from **II**: 0.34 g of isomer mixture **IIa**/**IIa′**, yield 40%; from **III**: 0.19 g of isomer mixture **IIIa**/**IIIa′** and 0.11 g of **IIIb**, ratio **IIIa**/**IIIa′**:**IIIb** = 63:37, overall yield 40%.

(2*E*,*Z*)-5-(3,3-Dimethyloxiran-2-yl)-3-methylpent-2-enal (Ia/Ia′). Colorless oil, $C_{10}H_{16}O_2$ (*M* 168.238). IR spectrum, ν, cm^{-1}: 2965, 2906, 1720, 1666, 1445, 1375, 1160. ^1H NMR spectrum (^1H–^1H COSY), δ, ppm: *E* isomer **Ia**: 1.27 s (3H, C^9H_3), 1.32 s (3H, C^8H_3), 1.67 s (3H, $C^{10}H_3$), 1.77 m (2H, 5-H), 2.3 m (2H, 4-H), 2.76 m (1H, 6-H). 5.93 d (1H, 2-H, *J* = 8 Hz), 9.99 d (1H, CHO, *J* = 8 Hz; *Z* isomer **Ia′**: 1.6 s (3H, $C^{10}H_3$), 5.85 d (1H, 2-H, *J* = 8 Hz), 9.97 d (1H, CHO, *J* = 8 Hz); the other signals were the same as for **Ia**. GC–MS data: retention time, min: 18.231 (**Ia**), 18.183 (**Ia′**); *m*/*z* (I_{rel}, %): isomer **Ia**: 168 (6) $[M]^+$, 153 (15) $[M - CH_3]^+$, 137 (2) $[M - CH_3O]^+$, 123 (5) $[C_9H_{15}]^+$, 95 (30) $[C_7H_{11}]^+$, 81 (100) $[C_6H_9]^+$, 71 (25) $[C_4H_7O]^+$, 41 (50) $[C_3H_5]^+$; isomer **Ia′**: 168 (3) $[M]^+$, 152 (3) $[M - O]^+$, 137 (10) $[M - CH_3O]^+$, 123 (15) $[C_9H_{15}]^+$, 95 (40) $[C_7H_{11}]^+$, 81 (100) $[C_6H_9]^+$, 71 (5) $[C_4H_7O]^+$, 41 (60) $[C_3H_5]^+$.

3-Methyl-3-(4-methylpent-3-en-1-yl)oxirane-2-carbaldehyde (Ib). Colorless oil, $C_{10}H_{16}O_2$ (*M* 168.238). IR spectrum, ν, cm^{-1}: 2987, 2933, 1715, 1645, 1149. ^1H NMR spectrum 1.23 s (3H, $C^{10}H_3$), 1.30 m (2H, 4-H), 1.62 s (3H, C^8H_3), 1.70 s (3H, C^9H_3), 2.15 m (2H, 5-H), 3.85 m (1H, 6-H), 5.10 br.s (1H, 2-H), 10.0 d (1H, CHO). GC–MS data: retention time 10.333 min; *m*/*z* (I_{rel}, %): 168 (1) $[M]^+$, 152 (15) $[M - O]^+$, 137 (20) $[M - CH_3O]^+$, 125 (5) $[C_9H_{17}]^+$, 123 (5) $[C_9H_{15}]^+$, 95 (40) $[C_7H_{11}]^+$, 82 (100) $[C_6H_{10}]^+$, 55 (15) $[C_4H_7]^+$, 41 (60) $[C_3H_5]^+$.

2,2,6-Trimethyl-1-oxaspiro[2.5]octan-4-one (IIa/IIa′). Colorless oil, $C_{10}H_{16}O_2$ (*M* 168.238). IR spectrum, ν, cm^{-1}: 2960, 2868, 1721, 1568, 1460, 1116, 1102. ^1H NMR spectrum, δ, ppm: α-isomer **IIa**: 1.06 d (3H, C^7H_3, *J* = 7 Hz), 1.22 s (3H, C^8H_3), 1.44 s (3H, C^9H_3), 1.86 m (1H, 5-H), 2.00 m (2H, 4-H), 2.18 d.d.d (1H, 3-H), 2.46 m (2H, 3-H, 6-H), 2.6 d (1H, 6-H); β-isomer **IIa′**: 1.09 d (3H, C^7H_3, *J* = 6 Hz), 1.23 s (3H, C^8H_3); the other signals were the same as for isomer **IIa**. ^{13}C NMR spectrum, δ_C, ppm: α-isomer **IIa**: 18.6 (C^7H_3), 19.3 (C^8H_3), 19.6 (C^9H_3), 21.7 (C^3), 29.7 (C^5), 32.7 (C^4), 42.7 (C^6), 49.2 (C^{10}), 63.2 (C^2), 206.3 (CO); β-isomer **IIa′**: 19.1 (C^7H_3), 19.4 (C^8H_3), 19.6 (C^9H_3), 26.0 (C^3), 30.4 (C^5), 33.7 (C^4), 42.7(C^6), 51.1 (C^{10}), 70.0 (C^2), 207.4 (CO). GC–MS data: retention time, min: 10.85 (**IIa**), 11.05 (**IIa′**); *m*/*z* (I_{rel}, %): α-isomer **IIa**: 168 (25) $[M]^+$, 153 (80) $[M - CH_3]^+$, 125 (20) $[C_7H_9O_2]$, 123 (5) $[C_7H_7O_2]^+$, 111 (50) $[C_6H_7O_2]^+$, 97 (10) $[C_7H_{13}]^+$, 86 (35) $[C_4H_6O_2]$, 70 (30) $[C_4H_6O]^+$, 43 (100) $[C_3H_7]^+$; β-isomer **IIa′**: 168 (5) $[M]^+$, 153 (80) $[M^+ - CH_3]$, 135 (10) $[M^+ - H_2O]$, 125 (5) $[(C_7H_9O_2]^+$, 111 (10) $[C_6H_7O_2]^+$, 97 (35) $[C_7H_{13}]^+$, 86 (5) $[C_4H_6O_2]^+$, 55 (20) $[C_4H_7]^+$, 43 (100) $[C_3H_7]^+$.

Oxidation of citral (I) and camphene (III) with *m*-chloroperoxybenzoic acid. A solution of 10 mmol of 80% *m*-chloroperoxybenzoic acid was carefully added in a dropwise manner over a period of 15 min to a solution of 5 mmol of compound **I** or **III** in 25 ml of chloroform at 0°C, and the mixture was stirred at room temperature under nitrogen, the progress of the reaction being monitored by TLC and peroxide test with a 10% solution of KI. The mixture was then carefully washed with a saturated aqueous solution of $NaHCO_3$ (3×10 ml) and distilled water (3×10 ml). The organic layer was separated, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure at room temperature, and the residue was subjected to column chroma-

tography on silica gel using petroleum ether (bp 60–80°C)–diethyl ether (9:2) as eluent to isolate 0.5 g (60%) of isomer mixture **Ia**/**Ia′** (from **I**) or 0.57 g (75%) of isomer mixture **IIIa**/**IIIa′** as a viscous oil.

3,3-Dimethylspiro[bicyclo[2.2.1]heptane-2,2′-oxirane] (IIIa/IIIa′). Colorless oil, $C_{10}H_{16}O$ (*M* 152.238). IR spectrum, ν, cm^{-1}: 2966, 2868, 1649, 1465, 1347, 1100. ^1H NMR spectrum, δ, ppm: *endo* isomer **IIIa**: 0.8 s (3H, C^9H_3), 0.89 s (3H, $C^{10}H_3$), 1.13 m (2H, 7-H), 1.26 d.d (2H, 5-H), 1.37 m (2H, 6-H), 1.86 m (1H, 1-H), 1.96 br.s (1H, 4-H), 2.67 d (1H, 8-H, *J* = 4 Hz), 2.69 d (1H, 8-H, *J* = 4 Hz); *exo* isomer **IIIa′**: 0.81 s (3H, C^9H_3), 0.90 s (3H, $C^{10}H_3$), 1.17 m (2H, 7-H), 1.41 d.d (2H, 5-H), 1.45 m (2H, 6-H), 1.82 m (1H, 1-H), 1.99 m (1H, 4-H), 2.75 d (1H, 8-H, *J* = 5 Hz), 2.78 d (1H, 8-H, *J* = 5 Hz). GC–MS data: retention time 17.917–19.233 min; *m*/*z* (I_{rel}, %): 152 (5) $[M]^+$, 137 (50) $[M - CH_3]^+$, 123 (7) $[M - CO]^+$, 119 (5) $[M - C_2H_9]^+$, 109 (100) $[M - C_2H_3O]^+$, 108 (48) $[M - C_2H_4O]^+$, 94 (25) $[C_7H_{10}]^+$; 85 (80), 67 (80), 65 (15) $[C_5H_5]^+$.

Camphor (IIIb). Colorless crystals, mp 180°C, $C_{10}H_{16}O$ (*M* 152.238). IR spectrum, ν, cm^{-1}: 3456, 2949, 1704, 1445, 1047. ^1H NMR spectrum, δ, ppm: 0.84 s (3H, C^9H_3), 0.91 s (3H, $C^{10}H_3$), 0.96 s (3H, C^8H_3), 1.38 m (2H, 5-H), 1.69 d.d.d (2H, 6-H, *J* = 4, 9, 13 Hz), 1.84 d (1H, 3-H, *J* = 18 Hz), 1.94 m (1H, 4-H), 2.35 d.t (1H, 3-H, *J* = 4, 18 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.3 (C^8H_3), 19.1 (C^9H_3), 19.7 ($C^{10}H_3$), 27.0 (C^5), 29.9 (C^6), 43.0 (C^4), 43.6 (C^7), 48.0 (C^3), 57.7 (C^1), 219.7 (CO). GC–MS data: retention time 15.690 min; *m*/*z* (I_{rel}, %): 152 (95) $[M]^+$, 137 (30) $[M - CH_3]^+$, 123 (5) $[M - C_2H_5]^+$, 109 (70) $[M^+ - C_3H_7]$, 95 (20) $[M^+ - C_4H_9]$, 81 (100) $[M - C_5H_{11}]$, 67 (70) $[M - C_6H_{14}]$, 41 (30) $[C_3H_5]^+$.

Photosensitized oxygenation of natural terpenes I and II (*general procedure*). A solution of 0.01 mol of compound **I** or **II** in chloroform or ethanol containing the corresponding singlet oxygen sensitizer was irradiated at –5°C using a sodium lamp, a continuous stream of dry oxygen being passed through the solution at a low rate to avoid evaporation of the mixture. The solvent was removed under reduced pressure (15 mm) at 20°C, and the residue was subjected to column chromatography on silica gel using petroleum ether (bp 60–80°C)–diethyl ether (9:2) as eluent. In the reaction with citral (**I**) we isolated compounds **Ic** and **Id**, and in the reaction with pulegone (**II**), compounds **IIa**/**IIa′**, **IIb**, and **IIc**. The reaction conditions (solvent, sensitizer, reaction time) and yields of the photoproducts are given in table.

(2*E*,5*E*)-7-Hydroperoxy-3,7-dimethylocta-2,5-dienal (Ic). Colorless oil, $C_{10}H_{16}O_3$ (*M* 184.238). IR spectrum, ν, cm^{-1}: 3423, 2965, 2863, 1715, 1620, 1456, 1138. ^1H NMR spectrum, δ, ppm: 1.34 s (6H, C^8H_3, C^9H_3), 2.21 s (3H, $C^{10}H_3$), 2.95 d (2H, 4-H, *J* = 6 Hz), 5.65 m (1H, 5-H), 5.72 d (1H, 6-H, *J* = 12 Hz), 5.90 d (1H, 2-H, *J* =8 Hz), 8.10 s (1H, OOH), 9.96 d (1H, CHO, *J* = 8 Hz). GC–MS data: retention time 18.868 min; *m*/*z* (I_{rel}, %): 184 (1) $[M]^+$, 166 (5) $[M - H_2O]^+$, 151 (25) $[M - HO_2]^+$, 123 (30) $[C_9H_{15}]$, 108 (80) $[C_8H_{12}]^+$, 91 (35) $[C_7H_7]^+$, 79 (100) $[C_5H_3O]^+$, 43 (50) $[C_3H_7]^+$, 39 (40) $[C_3H_3]^+$.

(2*E*)-6-Hydroperoxy-3,7-dimethylocta-2,7-dienal (Id). ^1H NMR spectrum, δ, ppm: 1.71–1.76 m (8H, 5-H, C^9H_3, $C^{10}H_3$), 1.98 br.s (2H, 4-H), 3.32 m (2H, 8-H), 4.93 br.s (1H, 6-H), 4.97 d (1H, 2-H, *J* = 8 Hz), 8.05 s (1H, OOH), 9.97 d (1H, CHO, *J* = 8 Hz).

2-(1-Hydroperoxy-1-methylethyl)-5-methylcyclohex-2-en-1-one (IIb). Colorless oil, $C_{10}H_{16}O_3$ (*M* 184.238). IR spectrum, ν, cm^{-1}: 3442, 2956, 2871, 1662, 1110. ^1H NMR spectrum, δ, ppm: 1.07 d (3H, C^7H_3, *J* = 7 Hz), 1.38 s (3H, C^8H_3), 1.46 s (3H, C^9H_3), 1.68 d.d.d.d (1H, 4-H, *J* = 3, 10, 10, 18 Hz), 2.03 d.d (1H, 6-H, *J* = 3, 10 Hz), 2.15 m (2H, 5-H, 6-H), 2.36 d.d.d.d (1H, 4-H, *J* = 3.6, 5, 5, 18 Hz), 3.49 br.s (1H, OH), 5.51 d.d (1H, 3-H, *J* = 3, 3.6 Hz), 8.8 s (1H, OOH). ^{13}C NMR spectrum, δ_C, ppm: 21.24 (C^7H_3), 25.48 (C^8H_3), 25.61 (C^9H_3), 28.28 (C^5), 33.63 (C^4), 38.60 (C^6), 82.30 (C^{10}), 119.56 (C^3), 149.80 (C^2), 199.53 (CO). GC–MS data: retention time 16.626 min: *m*/*z* (I_{rel}, %): 184 (2) $[M]^+$, 166 (6) $[M - H_2O]^+$, 153 (100) $[M - CH_3O]^+$, 137 (15) $[M - CH_3O_2]^+$, 135 (15) $[M - CH_5O_2]^+$, 94 (5) $[C_6H_6O]^+$, 66 (5) $[C_5H_6]^+$, 43 (35) $[C_3H_7]^+$.

2-Hydroperoxy-5-methyl-2-(1-methylethenyl)-cyclohexan-1-one (IIc). Colorless oil, $C_{10}H_{16}O_3$ (*M* 184.238). IR spectrum, ν, cm^{-1}: 3418, 2960, 2871, 1704, 1451, 1160. ^1H NMR spectrum, δ, ppm: 1.00 d (3H, C^7H_3, *J* = 6 Hz), 1.4 m (2H, 4-H), 1.80 s (3H, C^8H_3), 2.00 m (1H, 5-H), 2.2 m (2H, 3-H), 2.5 m (2H, 6-H), 5.0 d (1H, 9-H, *J* = 20 Hz), 5.15 d (1H, 9-H, *J* = 20 Hz), 9.85 s (1H, OOH). ^{13}C NMR spectrum, δ_C, ppm: 18.0 (C^8H_3), 19.0 (C^7H_3), 21.5 (C^3), 28.5 (C^5), 31.3 (C^4), 47.7 (C^6), 116.8 (C^2), 119.5 (C^9), 141.6 (C^{10}), 208.0 (CO). GC–MS data: retention time 19.053 min; *m*/*z* (I_{rel}, %): 184 (2) $[M]^+$, 166 (50) $[M - H_2O]^+$, 152 (100) $[M - CH_2O]^+$, 137 (35) $[M - CH_3O_2]^+$, 135 (15) $[M - CH_5O_2]^+$, 95 (60) $[C_6H_7O]^+$, 81 (99) $[C_5H_5O]^+$, 66 (10%) $[C_5H_6]^+$, 43 (30) $[C_3H_7]^+$.

Study on photoinduced DNA damage in the presence of hydroperoxides Ic and 2b. A solution of DNA in saline, 1 ml, was added to a solution of 1 mg of hydroperoxide **Ic** or **2b** in 5 ml of ethanol. The mixture was irradiated for 8 h at 0°C using a sodium lamp, and samples were withdrawn at definite time intervals to determine the damaging effect by the gel electrophoresis technique [24]. The photographs of the gel were taken under UV light (λ = 365 nm). Compound **Ic** induced a moderate degree of DNA damage after irradiation for 8 h, and compound **IIb** showed a moderate degree of DNA damage after irradiation for 5 h and high degree of DNA damage after irradiation for 8 h.

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