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UV irradiation of arylidene-β-ionones in the presence of dioxygen: regioselective formation of stable endoperoxides

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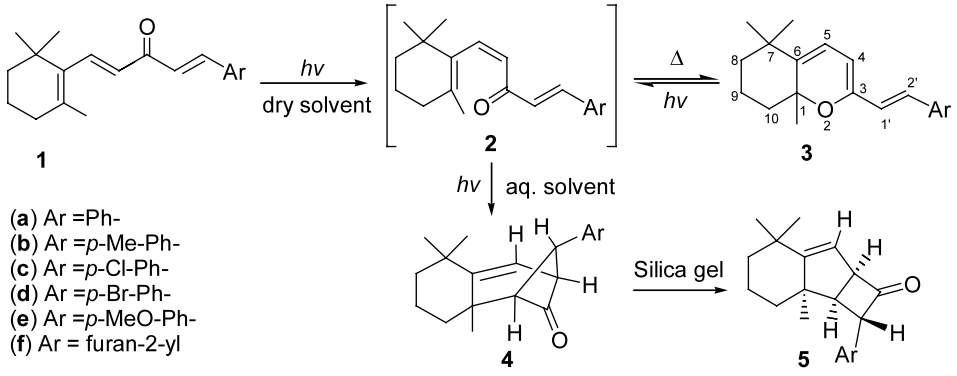
Abstract—UV irradiation of (*E*,*E*)-arylidene-β-ionones **1** leads to photoisomerization resulting in (*Z*,*E*) arylidene-β-ionones **2**, which undergo electrocyclization to 1,7,7-trimethyl-3-(*E*-2′-arylethenyl)-2-oxabicyclo[4.4.0]deca-3,5-dienes **3**, and the latter in the excited state add regioselectively, involving only the electron-rich endocyclic diene, to molecular oxygen affording highly stable endoperoxides **6**.

Endoperoxides, which are produced by the addition of molecular oxygen to cyclic dienes and arenes are not only intermediates in phototransformations of some natural products[1] but are also valuable precursors to a variety of molecules.[2] The biological activity of some natural endoperoxides like artemisinin (antimalarial),[3] ascaridole (anthelmintic)[4] and a variety of physiologically active prostaglandin-endoperoxides[5] has been attributed to the presence of the endoperoxide moiety. Recently, much attention has been focused on the isolation of stable endoperoxides,[6] which can serve as useful sources of singlet oxygen under thermal/photochemical conditions.[7] We have recently reported that irradiation of (*E*,*E*)-arylidene-β-ionones **1a**–**f** in anhydrous solvents leads to the formation of 1,7,7-trimethyl-3-(*E*-2′-arylethenyl)-2-oxabicyclo[4.4.0]-deca-3,5-dienes **3a**–**f**, ~90%, which on irradiation in aqueous methanol are converted to 11-(*exo*)-aryl-1,7,7-trimethyl-tricyclo[4.4.0.1^{2,4}]undec-5-ene-3-ones **4a**–**f** (Scheme 1), and the latter rearrange, quantitatively, on silica gel to 5-aryl-7,11,11-trimethyl-tricyclo[5.4.0.0^{3,6}]undec-1-ene-4-ones **5a**–**e**.[8]

In view of the report that certain electron rich systems undergo photocycloadditions with dioxygen without the use of any singlet-oxygen-sensitizer to generate the endoperoxides[6c] and known thermal routes to endoperoxides under electron-transfer conditions,[4a,b,9] it was decided to irradiate (*E*,*E*)-arylidene-β-ionones **1** under an oxygen atmosphere to investigate the possible



Scheme 1.

Keywords: UV irradiation; endoperoxides; arylidene-β-ionones; pyrans; electron-transfer.

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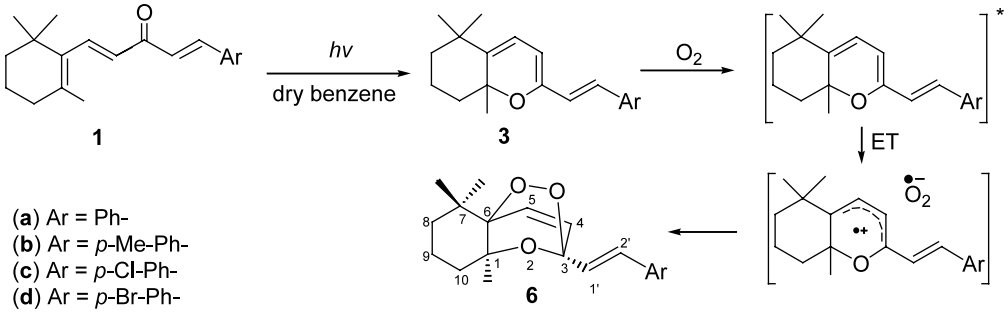

Scheme 2.

cycloaddition of the electron rich conjugated-π system in **3** (generated in situ) with molecular oxygen under photo-electron-transfer conditions. We report herein that in the presence of oxygen, the in situ generated dienes **3a–d** undergo photocycloaddition with molecular oxygen regioselectively to generate novel endoperoxides possessing a stable trioxane moiety.

Solutions of **1a–d** (400 mg) in dry benzene (250 mL) in an immersion well type Pyrex glass, water-cooled photoreactor were irradiated with a 125-Watt medium pressure Hg arc placed coaxially inside the reactor, in the presence of oxygen (continuously bubbled) for 45 min. Concentration of the resulting photolysates under reduced pressure using an Eyela rotary evaporator and column chromatographic resolution over silica gel (Acme Synthetic Chemicals, Mumbai, India, 60–120 mesh, 20 g, packed in hexane), using hexane–chloroform (9:1) as eluant, afforded endoperoxides **6a–d** (85–90%), which were characterized by rigorous spectroscopic analysis.[10]

The addition of a molecule of oxygen in the above phototransformation was indicated by the respective mass spectra of **6a–d**. The characteristic features of the ^{1}H NMR spectrum of **6a** were an AB quartet in the olefinic region (δ_A 6.70 and δ_B 6.58, $J_{AB}=8.64$ Hz, C4-H and C5-H) and the presence of two doublets at δ 6.95 ($J=16.25$ Hz, C2′-H) and δ 6.18 ($J=16.25$ Hz, C1′-H); the latter indicated the presence of an intact side chain olefinic moiety (as in **3**).[11] The ^{13}C NMR spectrum revealed three oxygen-linked carbon resonances at δ 94.61 (C3), δ 82.18 (C6) and δ 78.36 (C1). Overall, the ^{1}H and ^{13}C NMR assignments corroborated the assigned structures, which were also supported by their IR spectra. Stereochemically, the styryl moiety at C3 has to be *anti* to the dioxygen-bridge, whereas the orientation of the methyl at C1 has not been established, though, stability and mechanistic considerations suggest it to be *anti* to the bridge; the spectroscopic data did not indicate the presence of any isomeric products.

There are reports in the literature wherein addition of molecular oxygen to electron rich aromatic molecules under photochemical conditions in the absence of sensitizer for $^1O_2$ generation has been described[6c] and it is postulated that, probably, the substrate itself acts as a sensitizer. However, there are also reports on the thermal addition of $^3O_2$ to dienes under catalytic conditions that proceed through an electron transfer route.[4a] In the present case it is also believed that the reaction occurs through an electron-transfer interaction between photoexcited **3** and molecular oxygen (Scheme 2). Previously, Gandhi et al.,[12] have proposed such a photochemical reaction between in situ derived Vitamin-K_1–chromenol and molecular oxygen leading to a labile trioxane, however, earlier reports had negated involvement of such a product in photo-oxidative transformations of Vitamin-K_1.[1a,c,d] In any case, and to the best of our knowledge, this is the first example of a [2+4] photo-addition of oxygen to a pyran leading to a stable endoperoxide (trioxane).

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10. **6a**: Colorless crystals, yield 85%, mp 82–83°C (hexane); ν_{max} (KBr)/cm^{-1}: 1655 (m), 1594 (m), 1493 (m), 1448 (m–s), 1371 (s), 1327 (w–m), 1248 (s), 1194 (s), 1134 (m), 1069 (s), 1039 (s), 978 (s), 953 (s), 924 (s), 844 (m), 756 (s), 698 (s); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.43–7.22 (m, 5H, arom.-Hs), 6.95 (d, 1H, C2′-H, J=16.25 Hz), 6.64 and 5.86 (δ_A and δ_B for an AB quartet, 2H, J_{AB}=8.64 Hz, C4-H and C5-H) 6.18 (d, 1H, C1′-H, J=16.25 Hz), 2.35–1.05 (overlapping multiplets, with methyl singlets at δ 1.19, δ 1.16 and δ 1.06, altogether 15H); ^{13}C ($CDCl_3$, 50 MHz): δ 135.80 (q. arom.), 135.71 (olefinic-CH), 132.84 (olefinic-CH), 128.88 (olefin CH), 128.32 (arom. CH), 126.19 (arom. CH), 123.09 (olefinic CH), 94.61 (C3), 82.18 (C6), 78.36 (C1), 35.76 (C7), 34.76 (CH_2), 34.63 (CH_2), 26.83 (CH_3), 25.62 (CH_3), 24.60 (CH_3), 19.46 (C9); EI-Mass m/z: 313 (M$^+$+1, 28), 312 (M$^+$, 90), 296 (27), 280 (29), 265 (63), 252 (35), 186 (40), 131 (53), 109 (80), 103 (40), 77 (40), 69 (100). **6b**: Colorless crystals, yield 88%, mp 75–76°C (hexane); ν_{max} (KBr)/cm^{-1}: 1655 (m), 1591 (s), 1491 (m–s), 1458 (m), 1398 (m), 1377 (s), 1352 (m), 1246 (s), 1194 (m–s), 1138 (m), 1089 (m–s), 1080 (s), 1038 (m), 1010 (m), 982 (w–m), 972 (w–m), 953 (m), 939 (m), 922 (m–s), 843 (m–s), 814 (m), 712 (m), 685 (s); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.32 (d, 2H, arom.-Hs, J=8.12 Hz), 7.12 (d, 2H, arom.-Hs, J=8.12 Hz), 6.94 (d, 1H, C2′-H, J=16.26 Hz), 6.70 and 5.58 (δ_A and δ_B for an AB quartet, 2H, C4-H and C5-H, J_{AB}=8.61 Hz), 6.14 (d, 1H, C1′-H, J=16.26 Hz), 2.35 (s, 3H, -PhC$\underline{H}_3$), 2.28–1.05 (overlapping multiplets, with methyl singlets at δ 1.20, δ 1.16 and δ 1.05, altogether 15H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 138.37 (q. arom.), 135.75 (olefinic CH), 132.88 (q. arom.), 132.76 (olefinic CH), 129.20 (arom. CH), 128.90 (olefinic CH), 126.93 (arom. CH), 121.77 (olefinic CH), 94.69 (C3), 82.21 (C6), 78.41 (C1), 35.72 (C7), 34.67 (CH_2), 34.57 (CH_2), 26.75 (CH_3), 25.55 (CH_3), 24.55 (CH_3), 21.23 (arom.-$\underline{C}H_3$), 19.39 (C9); EI-Mass m/z: 327 (M$^+$+1, 18), 326 (M$^+$, 60), 311 (24), 310 (17), 294 (20), 235 (32), 222 (34), 219 (22), 209 (31), 199 (35), 181 (53), 117 (21), 91 (31), 69 (100). **6c** Colorless crystals, yield 90%, mp 80–81°C (hexane); ν_{max} (KBr)/cm^{-1}: 1655 (m), 1591 (m), 1491 (m–s), 1458 (m), 1398 (w–m), 1385 (m), 1377 (m–s), 1352 (m), 1246 (s), 1194 (s), 1138 (m), 1089 (m–s), 1080 (s), 1038 (m), 1011 (m), 982 (m), 972 (w–m), 953 (m), 939 (m), 922 (m–s), 843 (m–s), 814 (m), 712 (m), 685 (s); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.36 (d, 2H, arom.-Hs, J=8.71 Hz), 7.29 (d, 2H, arom.-Hs, J=8.71 Hz), 6.92 (d, 1H, C2′-H, J=16.27 Hz), 6.62 (br s, 2H, C4-H and C5-H), 6.16 (d, 1H, C1′-H, J=16.27 Hz), 2.33–1.05 (overlapping multiplets with methyl singlets at δ 1.20, δ 1.15 and δ 1.05, altogether 15H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 137.50 (q. arom.), 134.47 (olefinic CH), 134.09 (q. arom.), 132.53 (olefinic CH), 129.05 (olefinic CH), 128.74 (arom. CH), 128.15 (arom. CH), 123.57 (olefinic CH), 94.44 (C3), 82.30 (C6), 78.48 (C1), 35.73 (C7), 34.63 (CH_2), 34.54 (CH_2), 26.72 (CH_3), 25.54 (CH_3), 24.53 (CH_3), 19.35 (C9); EI-Mass m/z: 348 (M$^+$+2, 22), 347 (M$^+$+1, 26), 346 (M$^+$, 71), 330 (23), 315 (19), 314 (24), 300 (16), 299 (51), 220 (22), 165 (33), 137 (20), 111 (18), 109 (70), 102 (20), 101 (19), 71 (34), 70 (18), 69 (100). **6d**. Colorless crystals, yield 90%, mp 83–84°C (hexane); ν_{max} (KBr)/cm^{-1}: 1655 (m), 1587 (m–s), 1487 (s), 1458 (m), 1398 (m), 1371 (s), 1298 (w), 1241 (m), 1194 (m), 1139 (w), 1071 (s), 1036 (m), 1006 (m), 977 (m), 950 (s), 920 (s), 888 (w), 842 (m), 815 (m), 741 (w), 703 (w); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.44 (d, 2H, arom.-Hs, J=8.70 Hz), 7.27 (d, 2H, arom.-Hs, J=8.70 Hz), 6.89 (d, 1H, C2′-H, J=16.27 Hz), 6.60 (br s, 2H, C4-H and C5-H), 6.16 (d, 1H, C1′-H, J=16.27 Hz), 2.31–1.03 (overlapping multiplets with methyl singlets at δ 1.18, 1.14 and 1.03, altogether 15H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 134.75 (olefinic CH), 134.51 (q. arom.), 132.09 (arom. CH), 131.70 (arom. CH), 129.05 (olefinic CH), 128.44 (arom. CH), 123.65 (olefinic CH), 122.63 (q. arom.), 94.43 (C3), 82.28 (C_6), 78.47 (C1), 35.72 (C7), 34.60 (CH_2), 34.52 (CH_2), 26.73 (CH_3), 25.54 (CH_3), 24.52 (CH_3), 19.35 (C9); ESI-Mass m/z: 416.5 (M$^+$+Na+2, 8), 415.5 (M$^+$+Na+1, 12), 414.5 (M$^+$+Na, 98), 412 (M$^+$+Na-2, 100).
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