SHORT PAPER

J. Chem. Research (S),
2000, 111–113

Olefin photoaddition to 4-oxoisophorone[†]

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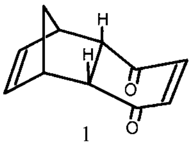
The first two examples of exclusive oxetane formation on olefin photoaddition to a cyclohex-2-en-1,4-dione, leading to two novel 2-substituted 3,3,6,8,8-penta-methyl-1-oxaspiro[3.5]non-5-en-7-ones are described herein

Since Albrecht[1] obtained the first known enedione (**1**), in 1906, these compounds have been the object of much research work, some of which helped shape organic chemistry as we know it nowadays (*viz.* the Diels–Alder reaction and the Woodward–Hoffmann rules).[2]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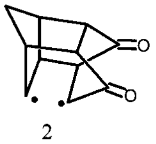
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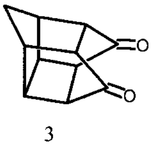
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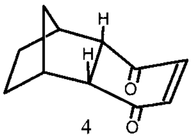
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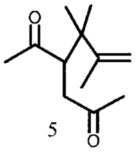
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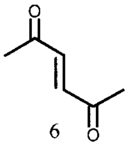
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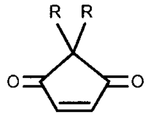
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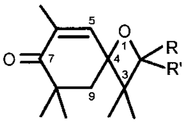
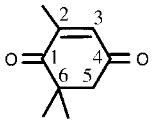

9 or 10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where: R = H or Me and R' = Me or Bu^t

The intramolecular photocyclization of the enedione moiety to the olefinic moiety in **1**, yielding the cage-compound **3**, was first described in 1964 by Cookson *et al.*[3] It has been extensively investigated since then, and is part of a proposed[4] solar-energy storage system. This reaction is not a concerted [2+2] cycloaddition and its mechanism ought to be formulated as in Scheme 1, in view of the cumulative results (see ref. 5a and references therein cited) published since 1964.

$$\mathbf{1} \xrightarrow{h\nu} {}^{1}[\mathbf{1}]_{1} \xrightarrow{\text{isc}} {}^{3}[\mathbf{1}]_{1} \longrightarrow {}^{3}[\mathbf{2}]_{1} \xrightarrow{\text{isc}} \mathbf{3}$$

Scheme 1

The involvement of the first excited triplet state of compound **1** (*i.e.* ${}^3[\mathbf{1}]_1$) is firmly established by now, by means of laser flash photolysis, sensitized irradiations and quenching studies.[5,6] On the other hand, although it was first proposed in 1966 by Dilling,[7] the biradical **2** still has not been observed spectroscopically, but its involvement is supported by investigations on the photoaddition of olefins to related polycyclic cyclohexenediones (**4** and its derivatives), by Barltrop and Giles,[6] as well as by the isolated open-chain by-product **5** obtained by Yoshida *et al.*,[8] on irradiating 3-hexene-2,5-dione (**6**) with tetramethylethylene (**TME**, 2,3-dimethylbut-2-ene). As it is derived from a triplet excited state (${}^3[\mathbf{1}]_1$), Dilling's biradical ought to be formed also as ${}^3[\mathbf{2}]_1$, before being converted to **3** (note that $\mathbf{3} \equiv {}^1[\mathbf{2}]_0$). Furthermore, the reversible formation of Dilling's intermediate might be the photochemical pathway for the deactivation of some sulfur and nitrogen substituted derivatives of **1**,[9] which do not photocyclize under prolonged UV irradiation.

Other intermediates are possible, however, besides Dilling's: Scheffer and Trotter's *tour-de-force* investigation[10] on both solution and crystalline phase photochemistry of tetrahydronaphthoquinones (compounds that are structurally related to **1**, but lack the methano bridge) revealed products the origin of which cannot be explained, unless one assumes the intermediacy[10] of a biradical, formed by intramolecular hydrogen abstraction by one of the carbonyl oxygens – after the (either singlet or triplet) excited state is attained – which then undergoes intramolecular radical recombination.

From the literature one also might be tempted to generalize the observation that enediones, on UV irradiation, in the presence of olefins, form cyclobutanes. However, Yoshida *et al.*[11] have shown that 4-cyclopentene-1,3-diones (**7**) do form oxetanes, instead of cyclobutanes, and Oda *et al.*[12] reported the formation of oxetanes as by-products on uv irradiation of 2-cyclohexene-1,4-dione, in the presence of **TME** or of (Z or E) 2-butene, in 30 and 3% yield, respectively. Scheffer and Trotter also reported[10] one case of oxetane formation, from a tetrahydronaphthoquinone lacking abstractable hydrogens.

In view of those facts, we reasoned that the formation of oxetanes might become the preferred reaction pathway, once the steric hindrance to attack at the enedionic double-bond becomes large enough, and set out in the quest for exclusive oxetane formation from enediones other than the 4-cyclopentene-1,3-diones. We now report the successful attainment of this goal.

Results and Discussion

We have found that UV irradiation (≥ 300 nm) of a benzene solution of 4-oxoisophorone (2,6,6-trimethyl-2-cyclohexene-1,4-dione, **8**), in the presence of a four-fold molar excess of **TME**, for 20h (Scheme 2) results in total conversion of **8** exclusively into the oxetane **9**. Longer irradiation times do result in the formation of secondary photoproducts, which we did not try to identify. In the ^{1}H NMR spectrum of **9**, the olefinic proton signal is present; in the ^{13}C NMR spectrum there are two olefinic carbon signals and a lone carbonyl signal is found at 203.63 ppm. These observations point unmistakably to the correctness of the structure for **9** as depicted in Scheme 2. If the olefinic photoaddition had taken place at the opposite carbonyl, the remaining carbonyl carbon signal ought to be less shielded than the observed value (in fact, for isophorone[13a] and cyclohex-2-en-1-one[13b] it is found at 198.5 and 198.7 ppm, respectively, while for compound **8** the carbonyl signals appear at 197.43 and 203.16 ppm).

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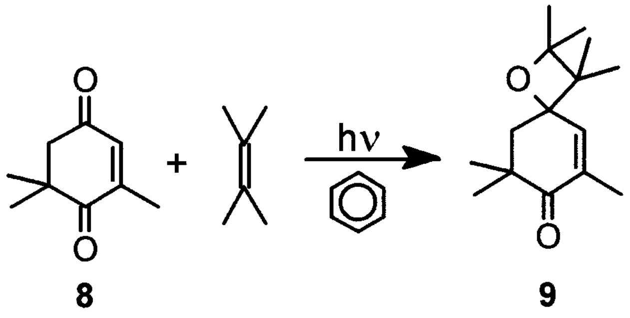
[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



Scheme 2

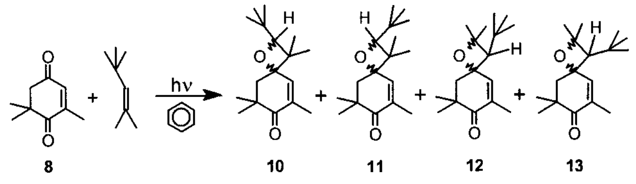
The complete regio- and chemo-selectivity in the formation of **9** nicely illustrates our steric-control hypothesis: that the *cooperative* steric hindrance existing between 4-oxoisophorone (**8**) and **TME** prevents the attack either at the enedionic double-bond or at the C-1 carbonyl moiety. The experiments described below provide further confirmatory evidence for this hypothesis.

UV irradiation (≥ 300 nm), for 20h, of a benzene solution of **8**, in the presence of a four-fold molar excess of trimethylethylene (β**IA**, β-isoamylene or 2-methyl-but-2-ene), instead of **TME**, leads to the formation of similar amounts (by capillary GC) of only eight (racemic) products (out of the twelve possible racemic diastereomers). When analysed by GC–MS, all eight products presented molecular-ion peaks at *m/z* 222. Moreover, of the said products, two also gave rise to peaks at *m/z* 164 [$M^{+\cdot}$ – Me^2CO] and two other products presented peaks at *m/z* 178 [M^b – MeCHO] – both characteristic of oxetanes – while the remaining four products exhibited peaks at *m/z* 194 [$M^{+\cdot}$ – CO] – typical of cyclobutanated enediones. Hence we imagine that here the products formed must have been the four head-to-head and the four head-to-tail adducts derived from attack at either the C-4 carbonyl moiety or the double-bond carbons, because the hindrance to attack at the other carbonyl should be sensibly higher. Nonetheless, this result shows that the cooperative steric hindrance between **8** and β**IA** is insufficient to prevent the attack at the enedionic double-bond.

However, the separation and characterization of the above mentioned eight products would entail a pointless exercise in preparative GC (or HPLC) purification, so we have forgone this avenue of investigation and changed the olefin once more, this time to the much more hindered β-isoöctene (β**IO**, 2,4,4-trimethylpent-2-ene).

We have found that UV irradiation (≥ 300 nm) of a benzene solution of **8**, in the presence of a four-fold molar excess of β**IO**, for 20h (Scheme 3), results in total conversion of **8** into the four oxetanes **10–13** (in the ratio of 9.8 : 5.1 : 3.6 : 81.5, by GC). Here also, longer irradiation times do result in the formation of secondary photoproducts, the identification of which was not pursued.

When analysed by GC–MS, all four products presented molecular-ion peaks at *m/z* 264. The two more abundant products also gave rise to peaks at *m/z* 178 [$M^{+\cdot}$ – Me_3CCHO], which are diagnostic of structures **10** and **11** (head-to-head addition), while both less abundant ones give rise instead to peaks at *m/z* 206 [$M^{+\cdot}$ – Me_2CO], indicative of head-to-tail addition (*viz.* **12** and **13**). Column chromatography followed by repetitive preparative TLC afforded a pure sample of the most abundant product. In its ^{13}C NMR spectrum there are two olefinic carbon signals and a lone carbonyl signal is found at 203.52 ppm. In the ^{1}H NMR spectrum of this product, the olefinic and oxetane proton signals appear, respectively, at 7.08 and 4.15 ppm. $^{1}H–\{^{1}H\}$ (1D) NOE difference experiments revealed a 2% enhancement at the 7.08 ppm signal on irradiation at 4.15 ppm, while irradiating at 7.08 ppm resulted in 1% enhancement at the 4.15 ppm signal, thus indicating that the olefinic and oxetane protons are proximal. These results led us to assign to this compound the structure **10** depicted in Scheme 3 (*i.e.* the *like*[15] diastereomer of the head-to-head adduct).



Scheme 3

It should be pointed out that the first vertical ionization potentials[18] of **TME** and β**IA** are 8.27 and 8.68 eV, respectively, and that of β**IO** can be estimated at 8.40 eV, in view of the published data[18] on related olefins. Thus, we believe that the electron-donor characteristics of all the olefins employed in this investigation are similar enough and ought not be regarded as a contributing factor to the observed reactivity.

Also, with regard to the nature of the excited states of 4-oxoisophorone (**8**), the first singlet excited state is[5a] (n→π*), and there is a consensus in the literature[6,10] that for cyclohexenediones the first triplet excited state is (π→π*). However, (π→π*) excited states of enones, enediones and quinones usually react with olefins forming cyclobutanes, because most of the electron density of these states is concentrated in the carbons of the double-bond, but that does not mean that the electron density at the carbonyls is zero, so that if the attack at the double-bond carbons is prevented by steric hindrance, the probable outcome will be oxetane formation through attack at the conjugated carbonyl. On the other hand, one might suggest that the $^{3}(\pi\rightarrow\pi^*)_1$ state of the enedione might be rendered ineffectual by the steric hindrance to the attack at the double-bond carbons, and that the formation of the oxetanes described in the present work ought, instead, to be due to the $^{1}(n\rightarrow\pi^*)_1$ state. We feel this second hypothesis is unlikely, the more so as the main reactive mode of the first excited singlet states of enediones is hydrogen abstraction and we did not find any trace of products attributable to such a reaction, although all the olefins employed have easily abstractable allylic hydrogens.

Conclusions

Having demonstrated that the outcome of olefin-cyclohexenedione photoaddition can be exclusive oxetane formation when there is sufficient steric hindrance to cyclobutane formation, we also confirmed Scheffer and Trotter's hypothesis[10] that the formation of this kind of product is the last-resort reactive pathway for deactivation of the enedione excited-state.

Experimental

Enedione **8** (Aldrich, 98%) was dissolved in an equal volume of *n*-hexane (Aldrich, P.A.) and crystallized from this solution overnight in a freezer. The crystals thus obtained were repeatedly recrystallized at low temperature from the same solvent until a 99.5% purity (by ^{1}H NMR and by GC) was attained (and its mp[16] = 16 °C). All other reagents (Aldrich) and solvents (Aldrich, Gold Label) were dried over anhydrous magnesium sulfate and used without further prior purification.

^{1}H and ^{13}C NMR spectra (at 200.13 and 50.32 MHz, respectively) were acquired on a Bruker AC-200-F, as described elsewhere.[17] All measurements were performed in 5 mm o.d. tubes, using a deuterium lock, at 20 °C, the samples being prepared by dissolving *ca* 50 mg of each oxetane in 0.5 mL of $CDCl_3$, containing 0.01 % $^{v}/v$ of TMS as internal standard.

All GC analyses were performed on a Shimadzu GC-14-A chromatograph, using a splitter injector (80:1, 230 °C), a 25 m × 0.25 mm

× 0.22 µm CBP–1 polydimethylsilicone gum capillary column, helium as carrier gas (1.6 mL min^{-1}) and a flame ionization detector (280 ºC, make up gas: N_2). Oven temperature program: 80 ºC (4 min), 20 ºC min^{-1} (up to 180 ºC), 180 ºC (3 min), 20 ºC min^{-1} (up to 250 ºC), 250 ºC (3 min). In these conditions compound **8** has t_R = 6.54 min. Data were collected with a Chromatopac C-R4A computer. GC-MS analyses were performed using a Finnigan-Mat INCOS-50 quadrupole mass spectrometer interfaced to a Varian 3400 gas-chromatograph, using settings analogous to those employed for analytic GC and a similar column.

A Perkin-Elmer 2400 CHN instrument was used to perform all elemental analyses.

General Procedure: A solution of 0.91cm^3 (6.2 mmol) of 4-oxoisophorone (**8**) and 27.0 mmol of the olefin in 25 cm^3 of dry benzene, contained in a 9 × 3.5 cm Pyrex tube, was deoxygenated by sonicating under a slow (benzene saturated) argon current for 15 min. It was irradiated with a (679A36) 450 W Hanovia Hg lamp during 20h, the solvent and excess olefin removed under reduced pressure, and the resulting yellow oil purified by flash-chromatography on silica-gel 60 (220–400 mesh) using dry benzene/hexanes (1:1) as the eluent. After solvent removal, the oxetanes were obtained as light-yellow oils, which did not crystallize and decomposed on attempted distillation.

2,2,3,3,6,8,8-heptamethyl-1-oxaspiro[3.5]non-5-en-7-one (**9**): When the olefin was **TME**, the above procedure afforded pure (99.7% by GC) **9**. Yield: 84% (isolated). Found: C, 76.1%; H, 10.2% ($C_{15}H_{24}O_2$ requires: C, 76.23%; H, 10.23%). ^{1}H NMR δ: 1.09 (3H, s, Me-3), 1.17 (6H, s, 2 x Me-8), 1.22 (3H, s, Me-2), 1.34 (3H, s, Me-3), 1.40 (3H, s, Me-2), 1.81 (3H, d, *J* = 0.83 Hz, Me-6), 2.12 (1H, d, *J* = 14.44 Hz, H-9), 2.20 (1H, d, *J* = 14.44 Hz, H-9), 6.90 (1H, bs, H-5). ^{13}C NMR δ: 16.24 (Me-6), 20.21 and 20.60 (Me-2 and Me-3), 26.14, 26.38, 26.48 and 26.58 (Me-2, Me-3 and 2 x Me-8), 40.93 (C-8), 44.45 (C-3), 45.16 (C-9), 80.28 (C-2), 83.40 (C-4), 133.62 (C-6), 143.04 (C-5), 203.63 (C-7). *m/z* ([assignment], rel. int. %): 236 ($M^{+\cdot}$, 0.22), 221 ($M^{+\cdot}$ – $Me^{\cdot}$, 0.32), 193 (0.18), 178 ($M^{+\cdot}$– Me_2CO, 8.85), 163 (32.81), 150 (2.56),135 (22.87), 84 (100.00), 69 (54.39). t_R = 11.10 min.

2-(*l*)-(*tert*-butyl)-*3,3,6,8,8-pentamethyl-1-oxaspiro[3.5]non-5-en-7-one* (**10**): When the olefin was β**IO**, the above procedure afforded four diastereomers. The mixture was applied to a 2 mm thick Silica-Gel 60 (20 x 20 cm, Merck), being resolved by eluting 27 times with isoöctane, whence pure (99.5% by GC) **10** was obtained. Yield: 65% (isolated). Found: C, 77.1%; H, 10.7% ($C_{17}H_{28}O_2$ requires: C, 7.22%; H, 10.67%). ^{1}H NMR δ: 0,97 (9H, s, Bu^t-2), 1.06 (3H, s, Me-3), 1.16 (6H, s, 2 × Me-8), 1.34 (3H, s, Me-3), 1.84 (3H, d, *J* = 0.91 Hz, Me-6), 1.96 (1H, d, *J* = 16.16 Hz, H-9), 2.19 (1H, d, *J* = 16.16 Hz, H-9), 4.15 (1H, s, H-2), 7.08 (1H, bs, H-5). ^{13}C NMR δ: 16.21 (Me-6), 19.59 (Me-3), 24.56 (Me-8), 25.73 (3 x Me in Bu^t-2), 26.11 and 26.67 (Me-3 and Me-8), 34.16 (C in Bu^t-2), 40.80 (C-8), 43.95 (C-3), 46.70 (C-9), 81.44 (C-4), 92.04 (C-2) 133.54 (C-6), 142.27 (C-5), 203.52 (C-7). *m/z* ([assignment], rel. int. %): 264 ($M^{+\cdot}$, 0.14), 249 (M^b – $Me^{\cdot}$, 0.14), 221 (0.17), 208 (0.42), 178 ($M^{+\cdot}$ – Bu^{t}CHO, 7.79), 163 (13.86), 150 (2.48),135 (21.40), 112 (34.99), 97 (100.00). t_R = 12.78 min.

Thanks are due to FAPESP (Procs 94/1773-0 and 92/1962-2), FINEP/PADCT II and CNPq for financial support and to Dr W. J. Baader for stimulating and fruitful discussions.

Received 6 October 1999; accepted 17 February 2000
Paper 99/55

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