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Photochemistry of 7,7-disubstituted 3,4,4*a*,5,6,7-hexahydro-4*a*-methyl-1(2*H*)-naphthalenones

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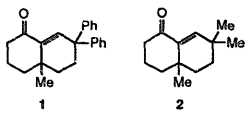
Abstract

The photochemistry of (±)-3,4,4*a*,5,6,7-hexahydro-4*a*-methyl-7,7-diphenyl-1(2*H*)-naphthalenone (**1**) and (±)-3,4,4*a*,5,6,7-hexahydro-4*a*,7,7-trimethyl-1(2*H*)-naphthalenone (**2**) is presented. Both molecules incorporate a rigid s-*cis* enone extended over two rings. In benzene, substrates **1** and **2** were photoinert. In alcohol solvents, hydrogen-bonded enols resulting from solvent addition to the enone double bond were isolated as the only photoproducts. The rearrangements anticipated for γ,γ-disubstituted enones, aryl migration for **1** and Type A rearrangement for **2**, were not observed. Spectroscopic and X-ray structure elucidation showed that solvent addition is highly regio- and stereospecific. Ketonization of the less hindered enols derived from **2** was observed upon heating or exposure to silica gel; enols produced from **1** were stable. Photolysis of **1** and **2** in aqueous dioxane led exclusively to β-hydroxy ketones. The mechanism leading to product formation was rationalized in terms of a stepwise addition of solvent to a triplet-derived ground state *trans* enone. A mechanism involving direct addition of solvent to a polarized excited state was also considered. © 1997 Elsevier Science S.A.

Keywords: s-*cis* enone; Triplet state; *cis–trans* photoisomerization; Photoaddition of alcohols; Hydrogen-bonded enols

1. Introduction

We have previously reported several extensions of the well known 4,4-diphenyl-2-cyclohexen-1-one photorearrangement [1,2]. These studies have documented the effects of (a) tethering the aryl groups which migrate during the reaction [3], (b) increasing the ring size [4], and (c) extending the conjugation of the chromophore [5]. In all of these studies, the enone moiety was built into a cyclic system and possessed the s-*trans* geometry. The current study sought to investigate the photochemistry of the s-*cis* enones (±)-3,4,4*a*,5,6,7-hexahydro-4*a*-methyl-7,7-diphenyl-1(2*H*)-naphthalenone (**1**) and (±)-3,4,4*a*,5,6,7-hexahydro-4*a*,7,7-trimethyl-1(2*H*)-naphthalenone (**2**). Although two cases of s-*cis* enones have been reported previously [6,7], naphthalenones **1** and **2** are the first photosubstrates to incorporate γ-disubstitution in an s-*cis* enone, introducing the possibility of aryl migration [1] in **1** and Type A rearrangement [2,8] in **2**. Here, we report the first study designed to explore the competitive reactions of s-*cis* enones.



1 **2**

2. Experimental details

2.1. Chemicals and equipment

Melting points (m.p.) are uncorrected. Infrared (IR) spectra are referenced to polystyrene. Unless otherwise indicated, ^1H and ^{13}C nuclear magnetic resonance (^1H NMR and ^{13}C NMR) spectra are reported in C_6D_6 at 400 MHz and 100 MHz, respectively, and are referenced to internal tetramethylsilane. High resolution mass spectra (HRMS, electron

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impact–direct probe) are reported at 70 eV. Elemental analyses (±0.3%) are given for stable compounds.

All reactions were carried out under an atmosphere of dry nitrogen. The solvents used in the photochemical runs were purified in the following manner: benzene was sequentially washed with concentrated H_2SO_4 (2×), 5% $KMnO_4$ in 10% H_2SO_4 (2×) and 10% aqueous KOH (1×), then dried over $MgSO_4$ and distilled from CaH_2; *t*-butyl alcohol and isopropyl alcohol were distilled from CaH_2; spectrophotometric grade methanol and dioxane were used as received. All photochemical reaction mixtures were degassed with dry oxygen-free nitrogen for 1 h prior to and during irradiation. Reactions were monitored by IR spectroscopy, thin layer chromatography (TLC) on silica gel or gas chromatography (GC) on a 6 m×0.25 mm SE-30 capillary column programmed between 50 °C and 300 °C. Photoproducts were purified by preparative thick layer chromatography (PTLC) on 20 cm×20 cm silica gel GF uniplates (Analtech, No. 02015) eluted with ether–hexane mixtures. TLC and PTLC band elution was monitored using a hand-held UV lamp.

The syntheses and spectra for (±)-3,4,4*a*,5,6,7-hexahydro-4*a*-methyl-7,7-diphenyl-1(2*H*)-naphthalenone (**1**) and (±)-3,4,4*a*,5,6,7-hexahydro-4*a*,7,7-trimethyl-1(2*H*)-naphthalenone (**2**) have been previously reported [9]. Following silica gel column chromatography, substrate **1** was recrystallized from ether–hexane; substrate **2** crystallized slowly to a low-melting solid and was used directly. The photosubstrates were stored under nitrogen at −20 °C in the absence of light.

2.2. *Irradiations. Purification and characterization of the products*

2.2.1. *General procedure for exploratory direct photolyses of (±)-3,4,4a,5,6,7-hexahydro-4a-methyl-7,7-diphenyl-1(2H)-naphthalenone (1) and (±)-3,4,4a,5,6,7-hexahydro-4a,7,7-trimethyl-1(2H)-naphthalenone (2)*

A solution of 100 mg of the naphthalenone (0.32 mmol for **1**; 0.52 mmol for **2**) in 175 ml of alcohol solvent in a 200-ml Kreil flask was irradiated through Pyrex using a 450 W medium pressure Hanovia immersion apparatus. The reactions were monitored by either IR or TLC and were stopped when further reaction progress was no longer detected; irradiation times ranged from 4.5 to 30 h. For reactions run in alcohol solvents, concentration under vacuum yielded an oil which was purified by PTLC eluted with 5–10% ether in hexane. For reactions run in dioxane–water (6:1), product isolation was achieved by concentrating the photolyzate under vacuum, extracting (3×) with 50 ml of ether, washing the extract with saturated aqueous NaCl (1×), drying (Na_2SO_4) and concentrating under vacuum. Final purification was effected by PTLC eluted with 10–20% ether in hexane. The following products were isolated from photolyses of **1**:

(±)-(4*aS**,8*S**)-8-*t*-Butoxy-2,3,4,4*a*,5,6,7,8-octahydro-4*a*-methyl-7,7-diphenyl-1-naphthol (**3a**). After 30 h, 100 mg (0.26 mmol, 80% based on 100% conversion) was isolated as a white solid, m.p. 165–167 °C. IR ($CDCl_3$) 3246, 1672, 1599, 1494, 1395, 1372, 755, 697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.62 (s, 1 H), 7.45 (d, 2 H, J=7.7 Hz), 7.29–7.07 (complex, 8 H), 4.33 (t, 1 H, J=2.2 Hz), 2.72 (td, 1 H, J=13.8, 3.3 Hz), 2.30 (dt, 1 H, J=6.9, 4.1 Hz), 2.05 (dm, 1 H, J=17.0 Hz), 1.96 (dm, 1 H, J=17.0 Hz), 1.63 (m, 1 H), 1.52 (m, 1 H), 1.43 (dm, 1 H, J=12.9 Hz), 1.34 (dt, 1 H, J=13.3, 3.4 Hz), 1.23 (s, 3 H), 1.12 (m, 2 H), 0.75 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 147.8, 147.4, 144.6, 129.8, 129.4, 127.6, 127.1, 125.9, 125.5, 109.8, 80.4, 77.4, 56.3, 40.1, 37.6, 36.2, 33.7, 29.3, 26.3, 24.8, 18.2; HRMS m/z calculated for $C_{27}H_{34}O_2$: 390.2559; found: 390.2561. Analysis calculated for $C_{27}H_{34}O_2$: C, 83.08; H, 8.72; found: C, 83.19; H, 8.75.

(±)-(4*aS**,8*S**)-2,3,4,4*a*,5,6,7,8-Octahydro-8-isopropoxy-4*a*-methyl-7,7-diphenyl-1-naphthol (**3b**). After 10 h, 88 mg (0.24 mmol, 77% based on 95% conversion) was isolated as a viscous, colorless oil. IR (thin film) 3265, 3086, 3056, 3021, 1670, 1599, 1495, 1385, 1374, 755, 698 cm^{-1}; ^1H NMR δ 9.73 (s, 1 H), 7.42 (d, 2 H, J=8.0 Hz), 7.30–7.12 (complex, 8 H), 4.32 (t, 1 H, J=2.3 Hz), 2.70 (td, 1 H, J=13.5, 2.3 Hz), 2.41 (septet, 1 H, J=6.2 Hz), 2.20 (dt, 1 H, J=13.9, 3.3 Hz), 2.09 (dm, 1 H, J=17.0 Hz), 1.98 (dm, 1 H, J=17.0 Hz), 1.70 (m, 1 H), 1.57 (m, 1 H), 1.41 (dm, 1 H, J=12.9 Hz), 1.32–1.21 (complex, 3 H), 1.23 (s, 3 H), 1.04 (d, 3 H, J=6.2 Hz), 0.79 (d, 3 H, J=6.2 Hz); ^{13}C NMR δ 147.8, 147.5, 143.9, 129.6, 128.9, 127.6, 127.4, 126.1, 125.6, 108.5, 87.0, 75.2, 56.0, 39.9, 37.2, 35.8, 33.3, 29.2, 25.0, 22.3, 20.1, 18.1; HRMS m/z calculated for $C_{26}H_{32}O_2$: 376.2402; found: 376.2408. Analysis calculated for $C_{26}H_{32}O_2$: C, 82.98; H, 8.51; found: C, 83.07; H, 8.58.

(±)-(4*aS**,8*S**)-2,3,4,4*a*,5,6,7,8-Octahydro-8-methoxy-4*a*-methyl-7,7-diphenyl-1-naphthol (**3c**). After 10 h, 60 mg (0.17 mmol, 77% based on 70% conversion) was isolated as a viscous, colorless oil. IR (thin film) 3284, 3086, 3056, 3023, 1670, 1599, 1496, 1375, 756, 698 cm^{-1}; ^1H NMR δ 9.24 (s, 1 H), 7.41 (d, 2 H, J=8.1 Hz), 7.31–7.14 (complex, 8 H), 4.26 (t, 1 H, J=2.4 Hz), 2.89 (s, 3 H), 2.60 (td, 1 H, J=13.9, 3.5 Hz), 2.22 (dt, 1 H, J=14.0, 3.5 Hz), 2.10 (dm, 1 H, J=17.0 Hz), 2.01 (dm, 1 H, J=17.0 Hz), 1.70 (m, 1 H), 1.58 (m, 1 H), 1.43 (m, 1 H), 1.35–1.21 (complex, 3 H), 1.22 (s, 3 H); ^{13}C NMR δ 147.5, 147.4, 143.4, 129.6, 128.6, 127.7, 127.5, 126.1, 125.8, 106.8, 91.6, 60.4, 55.9, 39.8, 37.2, 35.7, 33.8, 29.0, 25.3, 18.1; HRMS m/z calculated for $C_{24}H_{28}O_2$: 348.2089; found: 348.2079. Analysis calculated for $C_{24}H_{28}O_2$: C, 82.76; H, 8.05; found: C, 83.03; H, 8.09.

(±)-(4*aS**,8*S**,8*aS**)-2,3,4,4*a*,5,6,7,8-Octahydro-8-hydroxy-4*a*-methyl-7,7-diphenyl-1(2*H*-naphthalenone (**4**). After 30 h, 20 mg (0.06 mmol, 37% based on 50% conversion) was isolated as a viscous, colorless oil which decomposed on standing. IR (thin film) 3533, 3088, 3056, 3031, 1694, 1599, 1494, 1318, 751, 701 cm^{-1}; ^1H NMR δ 7.52–7.12 (complex, 10 H), 4.80 (bs, 1 H), 2.86 (td, 1 H, J=13.6,

3.2 Hz), 2.69 (m, 2 H), 2.55 (td, 1 H, J=12.4, 6.5 Hz), 2.35 (t, 2 H, J=14.8 Hz), 1.87 (m, 2 H), 1.53 (dt, 1 H, J=14.0, 3.2 Hz), 1.20 (m, 2 H), 1.11 (d, 1 H, J=12.4 Hz), 0.78 (s, 3 H); ^{13}C NMR δ 216.2, 145.8, 144.0, 128.9, 128.7, 127.2, 127.1, 126.6, 126.0, 73.6, 56.9, 51.1, 40.5, 35.3, 34.4, 31.3, 29.4, 24.3, 20.3; HRMS m/z calculated for $C_{23}H_{26}O_2 - H_2O$: 316.1828; found: 316.1823. This compound was too unstable to obtain an acceptable elemental analysis.

The following products were isolated from photolyses of **2**:

(±)-(4a*S**,8*R**)-8-*t*-Butoxy-2,3,4,4*a*,5,6,7,8-octahydro-4*a*,7,7-trimethyl-1(2*H*)-naphthol (**5a**). After 4.5 h, 89 mg (0.33 mmol, 80% based on 80% conversion) was isolated as a viscous, colorless oil. IR (thin film) 3279, 1675, 1380, 1369 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.25 (s, 1 H), 3.95 (s, 1 H), 2.02 (m, 2 H), 1.64–1.41 (complex, 5 H), 1.39–1.20 (complex, 3 H), 1.23 (s, 9 H), 1.07 (s, 3 H), 0.93 (s, 3 H), 0.88 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 148.1, 108.8, 79.4, 75.7, 40.4, 38.1, 37.5, 36.7, 36.6, 29.4, 28.6, 27.4 (2), 24.5, 18.8 (2), 18.5; HRMS m/z calculated for $C_{17}H_{30}O_2$: 266.2246; found: 266.2240. Analysis calculated for $C_{17}H_{30}O_2$: C, 76.69; H, 11.27; found: C, 76.77; H, 11.30.

(±)-(4a*S**,8*R**)-2,3,4,4*a*,5,6,7,8-Octahydro-8-isopropoxy-4*a*,7,7-trimethyl-1(2*H*)-naphthol (**5b**). After 7 h, 65 mg (0.26 mmol, 55% based on 90% conversion) was isolated as a viscous, colorless oil. IR (thin film) 3297, 1674, 1382, 1373 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.23 (s, 1 H), 3.82 (s, 1 H), 3.69 (septet, 1 H, J=6.2 Hz), 2.03 (m, 2 H), 1.61 (m, 2 H), 1.45 (m, 2 H), 1.32–1.17 (complex, 4 H), 1.22 (d, 3 H, J=6.2 Hz), 1.21 (d, 3 H, J=6.2 Hz), 1.05 (s, 3 H), 0.96 (s, 3 H), 0.88 (s, 3 H); ^{13}C NMR δ 148.2, 107.2, 86.3, 74.5, 40.5, 38.5, 37.5, 36.2, 29.4, 27.8, 24.7, 22.4, 21.1, 18.7, 18.2; HRMS m/z calculated for $C_{16}H_{28}O_2$: 252.2089; found: 252.2086. Analysis calculated for $C_{16}H_{28}O_2$: C, 76.19; H, 11.11; found: C, 76.33; H, 11.20.

(±)-(4a*S**,8*R**)-2,3,4,4*a*,5,6,7,8-Octahydro-8-methoxy-4*a*,7,7-trimethyl-1(2*H*)-naphthol (**5c**). After 10 h, spectroscopic analysis of the crude photolyzate indicated the presence of an enol product [IR bands at 3340 and 1673 cm^{-1}; ^{1}H NMR signals at 8.92 (s, 1 H) and 3.10 (s, 3 H)]. This product was not stable, however, and PTLC purification resulted in rapid and complete conversion to methoxy ketone **6c** (see below).

(±)-(4a*S**,8*S**,8a*S**)-2,3,4,4*a*,5,6,7,8-Octahydro-8-hydroxy-4*a*,7,7-trimethyl-1(2*H*)-naphthalenone (**6d**). After 11 h, 61 mg (0.29 mmol, 63% based on 88% conversion) was isolated as a white solid, m.p. 96–98 °C. IR (thin film) 3449, 1692, 1382 cm^{-1}; ^{1}H NMR (70°C) δ 3.40 (bs, 1 H), 2.44 (quintet, 1 H, J=7.8 Hz), 2.17 (d, 1 H, J=4.8 Hz), 2.14 (m, 1 H), 1.93 (m, 1 H), 1.69–1.50 (complex, 3 H), 1.32 (m, 2 H), 1.12–0.95 (complex, 3 H), 0.87 (s, 3 H), 0.80 (s, 3 H), 0.78 (s, 3 H); ^{13}C NMR (70 °C) δ 215.3, 77.5, 58.4, 41.7, 36.7, 36.2, 34.3, 32.1, 29.3, 27.1, 25.5, 20.9 (2); HRMS m/z calculated for $C_{13}H_{22}O_2$: 210.1620; found: 210.1611. Analysis calculated for $C_{13}H_{22}O_2$: C, 74.28; H, 10.48; found: C, 74.25; H, 10.45.

2.2.2. *Single crystal X-ray structure determination of (±)-(4a*S**,8*S**)-8-t-butoxy-2,3,4,4a,5,6,7,8-octahydro-4a-methyl-7,7-diphenyl-1-naphthol (**3a**) and (±)-(4a*S**,8*S**,8a*S**)-3,4,4a,5,6,7,8,8a-octahydro-8-hydroxy-4a,7,7-trimethyl-1(2H)-naphthalenone (**6d**)*

Single crystals of **3a** and **6d** were mounted on a syntex P4 automated diffractometer. Unit cell dimensions (Table 1) [3] were determined by least squares refinement of the best angular positions for **3a** (58 independent reflections, $2\theta > 9.99°$) and **6d** (51 independent reflections, $2\theta > 10.2°$) during normal alignment procedures using molybdenum irradiation (λ=0.71073 Å). Data (7973 for **3a**, 3799 for **6d**, independent points after removal of space group forbidden and redundant data) were collected at room temperature using a variable scan rate, θ–2θ scan mode and a scan width of 1.2° below Kα_1 and 1.2° above Kα_2 to a maximum 2θ value of 45° for **3a** and 60° for **6d** [10]. Backgrounds were measured at each side of the scan for a combined time equal to the total scan time. The intensities of three standard reflections were measured every 97 reflections. As the intensities of these reflections showed less than 6% variation, corrections for decomposition were deemed unnecessary. Data were corrected for Lorentz, polarization and background effects. After removal of redundant and space group forbidden data, observed reflections (3116 for **3a**, 3788 for **6d**) were used for solution of carbon and oxygen positions of the structure by direct methods [11]. Refinement of scale factor, positional and anisotropic thermal parameters for all non-hydrogen atoms was carried out to convergence. Hydrogen positions were calculated using a C–H distance of 0.97 Å and idealized geometry and were included in the final refinement with fixed isotropic thermal parameters. A difference Fourier synthesis revealed no electron density of interpretable level. Scattering factors were taken from the International Tables [12]. The final cycle of refinement [function minimized $\Sigma(|F_o| - |F_c|)^2$] led to an agreement factor, R=6.13% for **3a**, 5.09% for **6d** [$R = (\Sigma||F_o| - |F_c||/\Sigma|F_o|) \times 100$]. In the final stages of refinement, a weight of $w^{-1} = \sigma^2(F) + 0.0008F^2$ was used for **3a** and $w = 1/[\sigma^2(F_o^2) + (0.0593p)^2 + 0.0p]$, where $p = (F_o^2 + 2F_c^2)/3$, was used for **6d**. R_w = 11.80% for **3a** and 10.45% for **6d**.

2.2.3. *Attempted irradiations in benzene*

Solutions of **1** (100 mg, 0.32 mmol) and **2** (80 mg, 0.42 mmol) in 175 ml of benzene in a 200-ml Kreil flask were irradiated through Pyrex using a 450 W medium pressure Hanovia immersion apparatus. TLC and GC indicated no

[3] Tables listing positional parameters, final anisotropic thermal parameters, bond angles and bond distances and calculated and observed structure factors are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK. Any request should be accompanied by a full literature citation.

Table 1
Crystal data for **3a** and **6d**

	3a	**6d**
Formula	$C_{27}H_{34}O_2$	$C_{17}H_{22}O_2$
Molecular weight	390.5	210.31
a/Å	19.54(2)	24.149(5)
b/Å	14.288(10)	6.208(1)
c/Å	18.048(16)	17.525(3)
α/deg	90.0	90.0
β/deg	116.10(7)	114.450(10)
γ/deg	90.0	90.0
V/(Å^3)	4527(7)	2445.3(8)
F(000)	1696	928
μ(Mo $K\alpha$)/mm^{-1}	0.070	0.075
λ(Mo $K\alpha$)/Å	0.71073	0.71073
D_{calcd}/(g cm^{-3})	1.146	1.142
Z	8	8
Independent reflections measured	7973	3799
Observed reflections	3116	3788
Octants measured	$\pm h, -k, +l$	$+h, +k, \pm l$
R/R_w (%)	6.13/11.80	5.09/10.45
Space group	$P2_1/c$	Cc
Goodness of fit	1.25	0.647

reaction and only minor decomposition after 30 h and 15 h, respectively.

2.2.3.1. Control experiments. Attempted acid- and base-catalyzed addition of methanol to 1 and 2

Solutions of **1** (100 mg, 0.32 mmol) and **2** (80.0 mg, 0.42 mmol) in 6.5 ml of 92 mM methanolic sodium methoxide (0.60 mmol) were stirred at room temperature in the absence of light. After 10 days, TLC showed no indication of a Michael adduct from either reaction. Careful neutralization and aqueous workup resulted in recovery (≥75%) of the starting enones. Similarly, treatment of **1** and **2** with methanol containing catalytic HCl gave no alcohol addition products.

2.2.4. Ketonization of enols 5b and 5c

A solution of 50 mg of each enol in 1 ml of $CHCl_3$ was applied to a silica gel PTLC plate. Each plate was stored under nitrogen in the dark at 20 °C for 4–48 h, at which time the compound was removed from the silica gel by extraction with ether. NMR analysis indicated that each ketone product was >95% pure. The following compounds were isolated: (±)-(4a*S**,8*S**,8a*S**)-3,4,4*a*,5,6,7,8,8*a*-Octahydro-8-isopropoxy-4*a*,7,7-trimethyl-1(2*H*)-naphthalenone (**6b**). After 2 days, ^{1}H NMR indicated an approximately 1:1 mixture of enol and ketone. The sample was heated under vacuum for 1.5 h at 45 °C to complete the conversion. The ketone (40 mg, 0.16 mmol, 80%) was isolated as a viscous, colorless oil which decomposed slowly on standing. IR (thin film) 1699, 1383, 1369 cm^{-1}; ^{1}H NMR δ 3.31 (septet, 1 H, J=6.1 Hz), 3.22 (dd, 1 H, J=4.1 Hz), 2.62 (dt, 1 H, J=15.6, 10.5 Hz), 2.41 (m, 2 H), 2.34 (dm, 1 H, J=4.1 Hz), 1.88 (td, 1 H, J=13.9, 4.3 Hz), 1.65 (m, 2 H), 1.30 (td, 2 H, J=13.9, 4.3 Hz), 1.23 (m, 2 H), 0.99 (d, 3 H, J=6.1 Hz), 0.90 (d, 3 H, J=6.1 Hz), 0.85 (s, 3 H), 0.75 (s, 3 H), 0.70 (s, 3 H); ^{13}C NMR δ 214.4, 82.1, 73.0, 58.9, 41.6, 36.7, 36.5, 35.0, 32.3, 30.6, 30.1, 28.9, 25.3, 23.5, 21.5, 21.4; HRMS m/z calculated for $C_{16}H_{28}O_2-C_3H_6O$: 208.1463; found: 208.1461. This ketone was too unstable to obtain an acceptable elemental analysis. Heating at 80 °C resulted in elimination to regenerate **2**.

(±)-(4a*S**,8*S**,8a*S**)-3,4,4*a*,5,6,7,8,8*a*-Octahydro-8-methoxy-4*a*,7,7-trimethyl-1(2*H*)-naphthalenone (**6c**). After 3 h, 44 mg (0.20 mmol, 88%) was isolated as a viscous, colorless oil which decomposed on standing. IR (thin film) 1698, 1385 cm^{-1}; ^{1}H NMR δ 2.94 (s, 3 H), 2.86 (d, 1 H, J=4.0 Hz), 2.43 (m, 3 H), 2.32 (m, 1 H), 2.27 (m, 1 H), 1.83 (td, 1 H, J=13.8, 4.7 Hz), 1.64 (m, 2 H), 1.40–1.13 (complex, 4 H), 0.84 (s, 3 H), 0.73 (s, 3 H), 0.65 (s, 3 H); ^{13}C NMR δ 213.7, 88.8, 57.9, 40.6, 36.1, 36.0, 34.7, 32.3, 30.0, 29.7, 28.0, 24.5, 23.4, 21.2; HRMS m/z calculated for $C_{14}H_{24}O_2-CH_4O$: 208.1463; found: 208.1460. This ketone was too unstable to obtain an acceptable elemental analysis. Heating at 80 °C resulted in elimination to regenerate **2**.

3. Results and discussion

3.1. Exploratory photochemistry and structural elucidation of the products

The photochemical reactions were carried out using conditions similar to those reported previously [3]. Compounds **1** and **2** gave no reaction when irradiated in benzene solution, but each gave a single photoproduct in *t*-butyl alcohol. At low conversion, the rate of photoproduct formation appeared linear with time, and each was produced in good chemical yield [80% from **1** (100% conversion); 80% from **2** (80% conversion)]. Each photoproduct showed strong IR absorptions at ≈3250 cm^{-1} and 1672 cm^{-1}; the C=C absorption of the starting enones was absent. The ^{1}H NMR spectra indicated the presence of an enolic proton at δ 9–10 and a *t*-butyl group in each product; the ^{13}C NMR spectra showed no carbonyl carbons. An X-ray structure determination of the product from **1** showed the interesting hydrogen-bonded enol (±)-(4a*S**,8*S**)-8-*t*-butoxy-2,3,4,4*a*,5,6,7,8-octahydro-4*a*-methyl-7,7-diphenyl-1-naphthol (**3a**) resulting from addition of solvent to the enone. Even though the enol double bond distorted the conformation of the ring system, it was clear that the alkoxy group in the product was *anti* to the C-4*a* angular methyl. Spectral comparison of **3a** with products from photolyses of **1** and **2** in other alcohol solvents suggested that all of the compounds had similar structures. Further irradiations of **1** and **2** in 6:1 dioxane:water led to the formation of products with substantially different spectral characteristics. Each product exhibited an O–H absorption at 3450–3550 cm^{-1} and a C=O at 1692 cm^{-1}. ^{1}H NMR showed no enolic protons and ^{13}C NMR confirmed the presence of a ketone in each compound. Conformational mobility in the product from enone **2**, however, resulted in broadened ^{1}H NMR signals (even at 70°C), and further proof of structure was required.

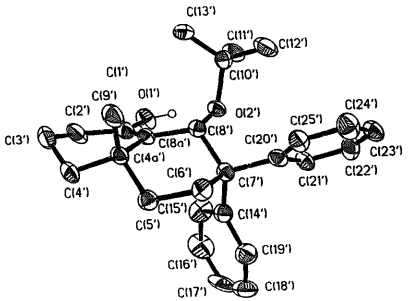


Fig. 1. Projection view of photoproduct **3a** (ellipsoids are shown at a 50% probability level).

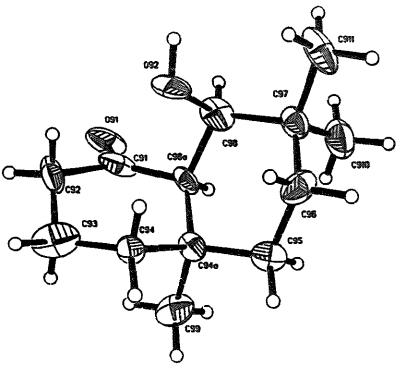


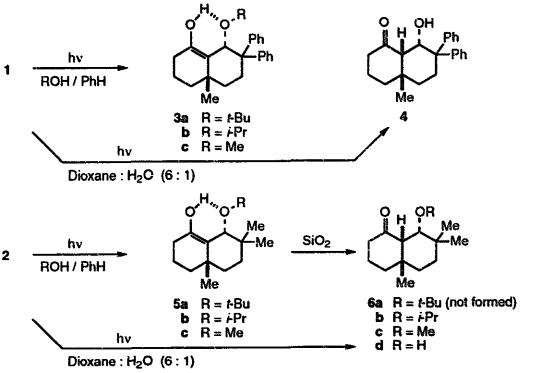
Fig. 2. Projection view of photoproduct **6d** (ellipsoids are shown at a 50% probability level).

X-ray analysis of the crystalline product from enone **2** showed it to be the *cis*-fused β-hydroxy ketone (±)-(4a*S**,8*S**,8a*S**)-3,4,4a,5,6,7,8,8a-octahydro-8-hydroxy-4a,7,7-trimethyl-1(2*H*)-naphthalenone (**6d**). As in the alcohol adducts, the hydroxy group in **6d** was *anti* to the angular methyl group. Comparison of ^{1}H NMR coupling patterns in **6d** allowed assignment of **4** as the water-addition product from photosubstrate **1**. The projection views [13] of photoproducts **3a** and **6d** are shown in Figs. 1 and 2. The photochemistry of **1** and **2** is summarized in Scheme 1.

3.2. Control experiments and ketonization of the enol products

The photoreactions of **1** and **2** afforded high yields of products resulting from alcohol addition to the enone. Since these products were also possible from simple Michael addition to the activated alkene, it was necessary to rule out this pathway. Substrates **1** and **2** were, therefore, stirred with methanol at 20 °C under both basic (excess NaOMe) and acidic (catalytic HCl) conditions for 10 days. Recovery of the starting enones in >75% yield from these experiments confirmed that the addition is a photochemical process.

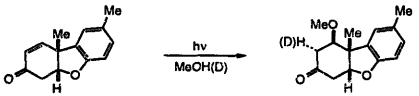
Two of the less hindered enols **5b** and **5c** proved to be unstable, gradually converting to the corresponding β-alkoxy ketones **6b** and **6c** upon mild heating or prolonged exposure to silica gel. Sterically hindered enols **3a–c** and **5a** were stable to these conditions. A two-dimensional nuclear Overhauser and exchange spectroscopy (2D-NOESY) experiment [14] performed on **6b** suggested a *cis* relationship between the hydrogens at C-8 and C-8a, and thus a *cis*-fused ring structure similar to that observed for **6d**. Further heating of **6b** and **6c** at 80 °C resulted in complete elimination of the alcohol and regeneration of enone **2**.



Scheme 1. The photochemistry of **1** and **2**.

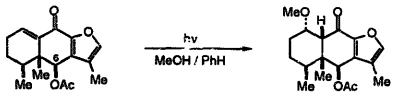
3.3. Mechanistic and interpretative discussion

The photochemistry of many cyclic s-*trans* enones (carbonyl and double bond s-*trans*) has been reported over the past 30 years. Reactions observed from these substrates included photoaddition of nucleophiles [2], photodimerization [2], photorearrangement [2], photoreduction [2] and photodeconjugation [15]. Previous studies have shown that solvent addition to cycloheptenone and cyclooctenone occurred in high yield and with high stereospecificity [16]; the yields of adducts from simple cyclohexenones, however, were considerably lower [17]. The lone report of a high-yield addition to a cyclohexenone was in the photochemistry of Pummerer's ketone (**7**) in methanol, which gave adduct **8** in 79% yield [18]. The stereochemistry in all of these reactions has been rationalized in terms of a *syn* addition of the alcohol to a triplet-derived ground state *trans* enone intermediate. Although *trans* cycloalkenone intermediates are well-accepted in medium-sized (≥7-membered) rings, the mechanism of addition to cyclohexenones is somewhat more controversial [2,19,20].



7 **8**

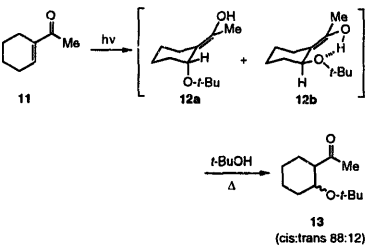
Only two photochemical studies of s-*cis* enones extended over two rings have appeared in the literature [6,7]. Of these, decompostin (**9**) [6] exhibited the closest structural similarity to **1** and **2** but lacked the γ(C-7)-disubstitution which would have made competitive aryl migration and Type A rearrangement possible. Upon photolysis in methanol, **9** yielded its 6-*epi*-methoxy derivative, but in 0.2% methanol–benzene, nucleophilic addition of solvent to the enone gave **10** as the only product in 95% yield. An X-ray structure of ketone **10** indicated not only an *anti* relationship between the methoxy group and the angular methyl but also a *cis*-fused ring junction. The authors postulated a mechanism involving addition of the alcohol to a strained *trans* enone intermediate.



9 **10**

In the current study, the photoreactions of **1** and **2** largely paralleled those of **9**, showing only solvent addition to the enone moiety. None of the expected aryl migration or Type A rearrangement was observed. In contrast to the results for **9**, the hydrogen-bonded enols **3** and **5** were isolated as the primary photoproducts. An analogous enol may also have been present in the photoreaction of **9**, but in the absence of bulky γ-substitution this could have rapidly ketonized under the reaction conditions or during purification. Indeed, the stability of the enol products from **1** and **2** increased as the groups flanking the alkoxy group on C-8 became larger.

Enols have been observed previously in the photochemistry of six-membered cyclic enones. Ramey and Gardner [21] found that irradiation of 1-acetylcyclohexene (**11**) in *t*-butyl alcohol gave the expected Michael-type adduct **13**. NMR analysis directly after irradiation, however, indicated the presence of a relatively long-lived enol which was easily ketonized upon heating to 80–85 °C. The formation of 2-*t*-butoxy-1-acetylcyclohexane in an 88:12 *cis*:*trans* ratio suggested the possibility of two enols, **12a** which ketonized rapidly and the hydrogen-bonded enol **12b** which converted more slowly. The preponderance of the *cis* ketone was attributed to steric constraints imposed by the *t*-butoxy group. A short-lived π,π^* excited triplet was thought to be responsible for the reaction, but the authors could not rule out the possibility of a triplet-derived *trans*-1-acetylcyclohexene intermediate.

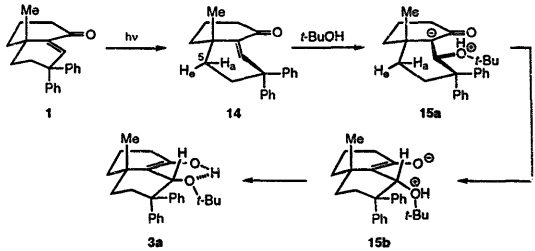


11 **12a** **12b**

13
(cis:trans 88:12)

Based on previous studies in the s-*trans* series, two mechanisms for photochemical solvent addition to s-*cis* enones **1** and **2** are possible: (A) stepwise addition of solvent to a triplet-derived ground state *trans* cycloalkenone intermediate [19] and (B) direct addition of solvent to a polarized excited state [8]. A third mechanism involving protonation of a π,π^* triplet followed by solvent capture [20] is unlikely, since this would be favored only under acidic conditions. Finally, the fact that isopropanol gives the same type of nucleophilic addition product as *t*-butyl alcohol with no enone photoreduction rules out a radical-mediated process [2,22].

In mechanism A (Scheme 2), the π,π^* excited triplet enone would undergo twisting of the C_α–C_β bond to minimize electron–electron repulsion. At some critical geometry, radiationless decay would occur to deliver the ground state *trans* enone **14**. The strained *trans* enone would be highly susceptible to nucleophilic attack, and although the π system would no longer have effective overlap, inductive polarization by the carbonyl should impart electropositive character to the β-carbon. In this intermediate, the steric environment around the strained double bond is somewhat deceptive. Molecular models suggest that the γ substituents would have a minimal impact on the addition process. Furthermore, the expected 1,3-nonbonded interaction between the incoming nucleophile and the angular methyl group is apparently not as important



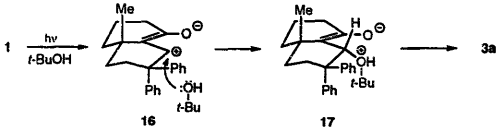
Scheme 2. Photoisomerization and addition of solvent to a strained *trans* enone.

as the shielding effect of the C-5 pseudoaxial proton (H_a) which effectively blocks attack from the α face of the molecule. Thus, solvent addition to **14** occurs *syn* to the angular methyl group to give dipolar intermediate **15a**. Conformational relaxation of **15a** to the less strained **15b** followed by protonation (intramolecular or intermolecular) at oxygen would then give enol **3a**. Previous studies [19] have proposed both concerted and stepwise variants for the mechanism of alcohol addition to *trans* enones. The fact that an enol is the primary photoproduct argues for a stepwise addition in the current reaction.

In mechanism B (Scheme 3), excitation to polar excited state **16** followed by addition of solvent to the β-electropositive carbon would generate intermediate **17**. Models suggest that the orientation of alcohol addition via this pathway would be controlled by the angular methyl group which would direct the solvent to approach from the opposite face of the molecule. The neighboring phenyl rings can flex out of the path of the incoming nucleophile and should have a minimal effect. Proton exchange in **17** would then give enol **3a** with the correct relative stereochemistry. Although this mechanism is possible, it seems unlikely, as the development of an electropositive center in **16** should lead to the formation of classical migration products in addition to the observed enols.

The photoaddition of alcohols to **1** and **2** proceeded in synthetically useful yields, comparable with other fused-ring s-*cis* enones [6,7]. Product regiochemistry was in accord with expectations based on polarization in the enone moiety, and the addition was highly stereospecific, with the added nucleophile positioned exclusively *anti* to the C-4*a* angular methyl. The isolation of enols, however, differed from the earlier studies of s-*cis* enones. The thermodynamic stability of the enol products seemed to correlate well with increased steric congestion in the adduct. Not only would the bulky groups tend to block the approach of potential proton donors, but steric interactions between the alkoxy group and the C-7 substituents would also stabilize the enol hydrogen bond by restricting conformational flexing of the ring. Beyond this, reference to models shows that ketonization of the enols requires eclipsing of the relatively large alkoxy group with one of the neighboring C-7 substituents as it moves to an axial position. This eclipsing is particularly unfavorable in the diphenyl-substituted enols **3a–c** and in the dimethyl *t*-butoxy enol **5a**; thus, these products are stable. Compounds **5b** and **5c**, however, are less hindered and ketonize to **6b** and **6c** under relatively mild conditions. The production of *cis*-fused products results from protonation on the less hindered face of the molecule, which is *syn* to the angular methyl once the alkoxy group assumes an axial orientation. The small amount of enone **2** found as a product in each of the ketonization reactions is readily explained by looking at the arrangement of groups in ketones **6b** and **6c**. In each structure, the alkoxy group adopts a *trans* diaxial relationship with the fused-ring (C-8*a*) hydrogen. Thus, mild heating readily promotes antiperiplanar elimination of the alkanol to regenerate the conjugated system.

In aqueous dioxane, only keto alcohols **4** and **6d** were isolated. Enols may be intermediates in the reaction, but they could not be detected in the crude photolyzate. Again these products can be rationalized in terms of mechanism A or B. When water is added, however, ketonization should be more facile, since the hydroxy group is small enough to tolerate eclipsing in the transition state as it moves to an axial position. It is also possible that the smaller water molecule gives a concerted *syn* addition to the *trans* enone. Finally, as in the ketonized alcohol addition products, elimination of water occurs at elevated temperatures to afford the starting enones.



Scheme 3. Direct addition to a polarized excited state.

4. Conclusions

The s-*cis* enones **1** and **2** have been shown to react in various alcohols to give regio- and stereospecific solvent addition products in synthetically useful yields. The primary products were isolated as hydrogen-bonded enols whose thermodynamic stability increased with the size of the added alkoxy group. Product structure assignments were confirmed by spectroscopic methods and X-ray analyses. No other processes involving aryl migration or Type A rearrangement were observed to compete with solvent addition. The mechanism for formation of these products most likely involved stepwise addition of solvent to an intermediate ground state *trans* enone. Stereochemistry in the final adducts was guided predominantly by steric effects. Ketonization was observed from less hindered enols derived from **2** to give *cis*-fused octahydro-1(2*H*)-naphthalenone products having the alkoxy *trans* diaxial to the fused-ring C-8*a* hydrogen. Upon heating, alcohol was readily eliminated from these ketonized products to regenerate the enone. In additions of water, ketone products were isolated; enol products, while likely intermediates, were not detected.

Acknowledgements

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