# Studies Directed toward the Synthesis of the Ingenane Diterpenes. An Unexpected Synthesis of *trans*-Bicyclo[5.3.0]decanes

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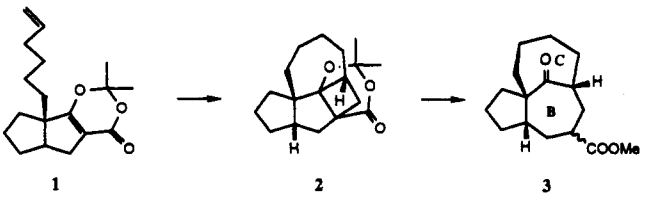
We have recently described the stereoselective synthesis of the carbocyclic ring system of the ingenane diterpenes, i.e., **3**, in which the highly unusual BC ring "inside–outside" or trans intrabridgehead stereochemical relationship[4,5] is established in the photocycloaddition of dioxenone **1** (Scheme I).[6]

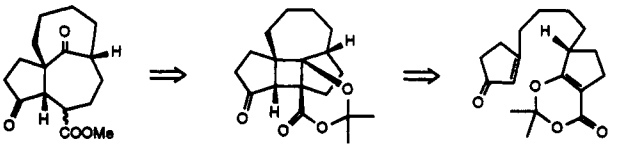
In an effort to explore the versatility of this photochemical methodology and at the same time examine the alternative, more convergent approach to the synthesis of the isomeric ingenane **4** outlined retrosynthetically below, **4** → **6** (Scheme II), the photocycloaddition of **6** has recently been examined. Unlike the intramolecular [2 + 2]photocycloaddition of **1**, the irradiation of **6** leads to a completely different reaction pathway that is the subject of this paper.

The requisite photosubstrate was prepared as shown in Scheme III. Addition of the alkyllithium derived from 4-[(*tert*-butyldimethylsilyl)oxy]-1-iodobutane to 3-ethoxycyclopentenone followed by acid hydrolysis[7] gave cyclopentenone **7** (87%). Luche reduction[8] of **7** (1.1 equiv of $CeCl_3 \cdot 7H_2O$, 1.1 equiv of $NaBH_4$, MeOH) followed by protection of the resulting allylic alcohol (0.1 equiv of PPTS, 2-methoxypropene as solvent, 67% overall yield from **5**) produced methoxypropenyl ether **8**. Conversion of **8** to iodide **9** was accomplished by successive removal of the *tert*-butyldimethylsilyl ether (1.5 equiv $Bu_4NF$, 87%), tosylation (1.3 equiv of TsCl, 0.1 equiv of DMAP, 3.0 equiv of triethylamine, $CH_2Cl_2$, 0 °C, quantitative), and halogenation (NaI, acetone, 25 °C, 58%). Reaction of iodide **9** with the dianion of cyclopentanone *tert*-butyl carboxylate then gave the β-keto ester **10** in 72% yield. Removal of the methoxypropenyl protecting group (0.1 equiv of PPTS, $H_2O$, THF, 0 °C, 63%) and oxidation (PDC, 86%) gave cyclopentenone **11** which upon treatment with trifluoroacetic acid, trifluoroacetic anhydride, and acetone was converted to dioxenone photosubstrate **6** in 52% yield.

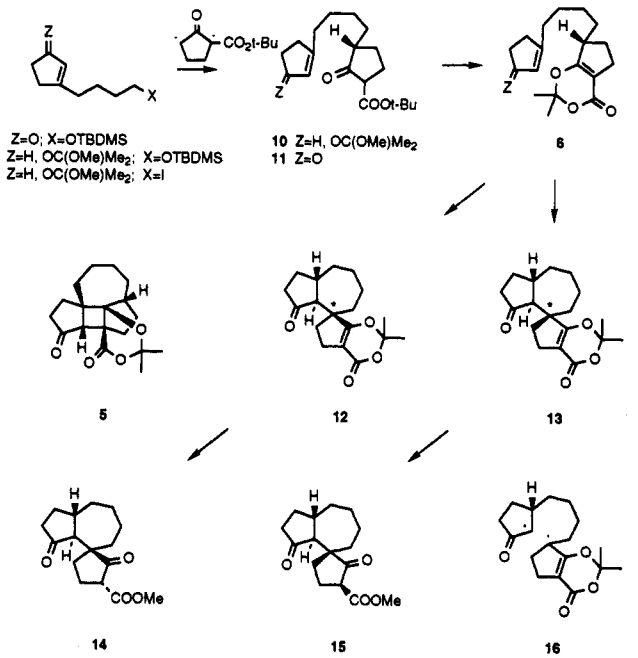
**Scheme I**



**Scheme II**



**Scheme III**




Irradiation of **6** (1.8 mM in degassed acetonitrile, 450-W medium-pressure Hanovia lamp, Pyrex filter) gave none of the desired dioxanone [2 + 2]photoadduct **5**, but instead led to the formation of an inseparable mixture of isomeric cycloadducts **12** and **13** in 88% yield. Subjecting this mixture to the conditions of acid fragmentation (catalytic *p*-TsOH in refluxing methanol, 18 h) provided two isomeric keto esters **14** and **15** (1:1.4 ratio), the structures and relative stereochemistries of which were confirmed by single-crystal X-ray analysis.[9]

These products presumably arise on irradiation of **6** by abstraction of the allylic hydrogen of the dioxenone by the cyclopentenone triplet, followed by collapse of the intermediate diradical **16** to give the isomeric dioxenones **12** and **13**. Intramolecular hydrogen abstraction by

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(3) Brown University. Author to whom correspondence regarding the X-ray structural data for **14** and **15** should be addressed.

(4) For a recent review describing inside–outside stereoisomerism, see: Alder, R. *Acc. Chem. Res.* **1983**, *16*, 321. For previous syntheses of inside-outside bicycloalkanes, see: (a) Winkler, J.; Hey, J.; Williard, P. *J. Am. Chem. Soc.* **1986**, *108*, 6425. (b) Winkler, J.; Hey, J.; Williard, P. *Tetrahedron Lett.* **1988**, 4691. (c) Gassman, P.; Korn, S.; Bailey, T.; Johnson, T.; Finder, J.; Clardy, J. *Tetrahedron Lett.* **1979**, 3401. (d) Haines, A.; Karntiang, P. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2577. (e) Gassman, P.; Thummel, R. *J. Am. Chem. Soc.* **1972**, *94*, 7183. (f) Park, C.; Simmons, H. *J. Am. Chem. Soc.* **1972**, *94*, 7184. (g) McMurry, J.; Hodge, C. *J. Am. Chem. Soc.* **1984**, *106*, 6450. (h) Gassman, P.; Hoye, R. *J. Am. Chem. Soc.* **1981**, *103*, 2498.

(5) Winkler, J. D.; Henegar, K. E.; Williard, P. G. *J. Am. Chem. Soc.* **1987**, *109*, 2850.

(6) For an alternative synthesis of the *trans*-bicyclo[4.4.1]undecane moiety of the ingenane diterpenes, see: Funk, R.; Olmstead, T.; Parvez, M. *J. Am. Chem. Soc.* **1988**, *110*, 3298.

(7) Becker, D.; Hardel, Z.; Nagler, M.; Gillon, A. *J. Org. Chem.* **1982**, *47*, 3297.

(8) Luche, J.-L.; Gemal, A. L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.

(9) Full details for the X-ray crystallographic data are included in the supplementary material.

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excited-state cycloalkenones is well-precedented,[10] although these reactions are exceedingly sensitive to reaction conditions.[10e] While the stereoselective formation of the *trans*-bicyclo[5.3.0]decane moiety is noteworthy, there appears to be little preference in the establishment of the third stereogenic center (starred carbon in **12** and **13**).

Further investigation of the application of the intramolecular dioxenone photocycloaddition reaction to the synthesis of the ingenane diterpenes is currently underway in our laboratory, and our results will be reported in due course.[11]

## Experimental Section

**General.** All solvents were reagent grade. Anhydrous THF was distilled from sodium. Organolithium reagents were obtained from Aldrich and standardized by titration with diphenylacetic acid. Merck precoated silica gel plates (250 μm) with fluorescent indicator were used for analytical TLC. Merck silica gel 60 (particle size 0.04–0.063 mm) was employed for flash chromatography. Melting points were obtained with a capillary melting point apparatus and are uncorrected. NMR spectra were measured at either 300 or 500 MHz. Most of the $^{13}C$ spectra have been studied by APT (attached proton test) to determine the number of protons attached to each carbon. Details of the X-ray crystallographic studies are included in the supplementary material.

**3-[4-[(*tert*-Butyldimethylsilyl)oxy]butyl]cyclopent-2-en-1-one, 7.** To a stirred solution of 4-(*tert*-butyldimethylsiloxy)-butyl iodide[12] (2.743 g, 8.73 mmol) in diethyl ether (26 mL) at −78 °C was added *tert*-butyllithium (9.15 mL, 19.21 mmol) in pentane. After stirring for 1 h at −78 °C, 3-ethoxycyclopentenone in diethyl ether (1 mL) was added dropwise, and the resulting mixture was allowed to warm to 25 °C. After 4 h, the reaction mixture was poured over ice and acidified to pH = 5 with 1 N HCl. The resulting solution was extracted twice with diethyl ether. The combined organic extracts were washed twice with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated under reduced pressure. The crude residue was purified by flash chromatography (15% ethyl acetate/petroleum ether) to yield the desired enone **7** (1.667 g, 78%): IR ($CDCl_3$) 2954, 2886, 1702, 1676, 1615, 1256, 1190, 836 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 0.05 (s, 6 H, $-Si(CH_3)_2$), 0.89 (s, 9 H, $-SiC(CH_3)_3$), 1.57 (m, 2 H), 1.67 (m, 2 H), 2.41 (m, 4 H), 2.58 (m, 2 H, $-CH_2(CO)-$), 3.64 (t, $J$ = 15 Hz, 2 H, $-CH_2OTBDMS$), 5.94 (s, 1 H, =CH–); MS (*m/z*, relative intensity) 269 (2), 253 (7), 211 (100), 165 (12), 129 (11), 119 (14); HRMS calcd for $C_{11}H_{19}O_2Si$ (M − t-Bu) 211.3587, found (M − t-Bu) 211.1154.

**1-[4-[(*tert*-Butyldimethylsilyl)oxy]butyl]-3-(1-methoxy-1-methylethoxy)cyclopentene, 8.** To a solution of enone **7** (2.46 g, 9.16 mmol) in methanol (2.5 mL) was added $CeCl_3·(H_2O)_7$ (3.75 g, 10.07 mmol) and $NaBH_4$ (0.381 g, 10.07 mmol). The resulting solution was stirred for 1.5 h at 25 °C and then poured into cold saturated aqueous $NaHCO_3$ and extracted three times with diethyl ether. The combined organic extracts were dried ($K_2CO_3$) and concentrated under reduced pressure to give crude allylic alcohol (2.15 g) which was used in the next step without further purification. Spectral data for the crude allylic alcohol: IR ($CDCl_3$) 3400, 2931, 2858, 1192, 1103, 839 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 0.05 (s, 6 H, $-Si(CH_3)_2$), 0.89 (s, 9 H, $-SiC(CH_3)_3$), 1.50 (m, 4 H), 1.70 (m, 1 H), 2.15 (m, 3 H), 2.29 (m, 3 H), 2.41 (m, 1 H), 3.60 (br s, 2 H, $-CH_2OTBDMS$), 4.81 (br s, 1 H, –CH(OH)–), 5.46 (s, 1 H).

To a stirred solution of the crude allylic alcohol (2.15 g, 7.96 mmol) in 2-methoxypropene (75 mL, 780 mmol) at 0 °C was added pyridinium *p*-toluenesulfonate (0.200 g, 0.796 mmol). After stirring 20 min at 0 °C, the reaction was treated with cold saturated aqueous $NaHCO_3$ and extracted twice with diethyl ether. The combined organic extracts were dried ($K_2CO_3$) and concentrated under reduced pressure. Flash chromatography of the crude residue (5% ethyl acetate/petroleum ether) gave the desired 2-methoxy-2-propyl ether **8** (2.08 g, 67% from starting enone): IR ($CDCl_3$) 2935, 2857, 1255, 1195, 836 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 0.05 (s, 6 H, $-Si(CH_3)_2$), 0.89 (s, 9 H, $-SiC(CH_3)_3$), 1.38 (s, 6 H, $-OC(CH_3)_2-$), 1.52 (m, 4 H), 1.75 (m, 1 H), 2.12 (m, 3 H), 2.25 (m, 1 H), 2.39 (m, 1 H), 3.21 (s, 3 H, $-OCH_3$), 3.60 (br s, 2 H, $-CH_2OTBDMS$), 4.85 (br s, 1 H, $-CH[OC(CH_3)_2(OCH_3)]$), 5.37 (s, 1 H, =CH–); MS (*m/e*, relative intensity) 341 (1), 195 (87), 187 (20), 149 (20), 133 (14), 121 (100), 105 (25); HRMS calcd for $C_{18}H_{34}O_2Si$ (M − HOMe) 310.5567, found (M − HOMe) 310.2351.

**1-(4-Iodobutyl)-3-(1-methoxy-1-methylethoxy)cyclopentene, 9.** To a stirred solution of silyl ether **8** (2.08 g, 6.09 mmol) in 5 mL of THF was added tetrabutylammonium fluoride (9.14 mL, 9.14 mmol) at 25 °C. After 30 min, the reaction was diluted with saturated aqueous $NaHCO_3$ and extracted three times with diethyl ether. The combined organic layers were dried ($K_2CO_3$) and concentrated under reduced pressure. Flash chromatography of the crude residue (50% ethyl acetate/petroleum ether) gave the deprotected primary alcohol (1.21 g, 87%): IR ($CDCl_3$) 3622, 2994, 2940, 2242, 1199, 1067, 1025 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.38 (s, 6 H, $-OC(CH_3)_2-$), 1.57 (m, 4 H), 1.75 (m, 1 H), 2.12 (m, 3 H), 2.25 (m, 1 H), 2.39 (m, 1 H), 3.21 (s, 3 H, $-OCH_3$), 3.64 (br s, 2 H, $-CH_2OH$), 4.85 (br s, 1 H, $-CH[OC(CH_3)_2(OCH_3)]-$), 5.36 (s, 1 H, =CH–); MS (*m/e*, relative intensity) 196 (3), 138 (9), 121 (10), 73 (100); HRMS calcd for $C_{12}H_{20}O_2$ (M − HOMe) 310.5567, found (M − HOMe) 196.1463.

To a solution of triethylamine (2.21 mL, 15.84 mmol), 4-(dimethylamino)pyridine (0.065 g, 0.53 mmol), and *p*-toluenesulfonyl chloride (1.11 g, 5.81 mmol) in $CH_2Cl_2$ (30 mL), at 0 °C, was added, dropwise, the above alcohol (1.21 g, 5.28 mmol) in $CH_2Cl_2$ (15 mL). After stirring for 16 h at 0 °C, the reaction mixture was diluted with diethyl ether and extracted twice with saturated aqueous $NH_4Cl$, twice with saturated aqueous $NaHCO_3$, and once with saturated aqueous NaCl. The organic layer was dried ($K_2CO_3$) and concentrated under reduced pressure to give 1.491 g of crude tosylate: IR (neat) 3180, 2970, 1476, 1370, 1188, 1039, 945, 821, 670 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.38 (s, 6 H, $-OC(CH_3)_2-$), 1.50 (m, 2 H), 1.65 (m, 2 H), 1.74 (m, 1 H), 2.08 (m, 3 H), 2.25 (m, 1 H), 2.34 (m, 1 H), 2.47 (s, 3 H, $-PhCH_3$), 3.21 (s, 3 H, $-OCH_3$), 4.02 (t, $J$ = 7.5 Hz, 2 H, $-CH_2OTs$), 4.82 (br s, 1 H, $-CH[OC(CH_2)_2(OCH_3)]-$), 5.31 (s, 1 H, =CH–), 7.32 (d, $J$ = 7.5 Hz, 2 H, $=CHC(CH_3)=$), 7.77 (d, $J$ = 7.5 Hz, 2 H, =CHC(OR)=); MS (*m/e*, relative intensity) 292 (11), 120 (93), 105 (44), 91 (100); HRMS calcd for $C_{16}H_{20}O_3S$ (M − $HOC(CH_3)_2OCH_3$) 292.3994, found (M − $HOC(CH_3)_2OCH_3$) 292.1133.

To a stirred solution of the above tosylate (1.491 g, 5.28 mmol) in acetone (11 mL) at 25 °C was added NaI (1.654 g, 11.04 mmol). After being stirred at 25 °C for 7.5 h, the reaction mixture was concentrated under reduced pressure. The residue was triturated with diethyl ether, and the resulting ethereal solution was then extracted twice with 10% sodium thiosulfate, once with water, and once with saturated aqueous $NaHCO_3$. Upon drying ($K_2CO_3$), the reaction was concentrated under reduced pressure. Flash chromatography of the crude residue (5% ethyl acetate/petroleum ether) gave iodide **9** (1.080 g, 58%): IR ($CDCl_3$) 2940, 1208, 1066 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.37 (s, 6 H, $-OC(CH_3)_2-$), 1.60 (m, 2 H), 1.70–1.90 (m, 3 H), 2.13 (m, 3 H), 2.26 (m, 1 H), 2.40 (m, 1 H), 3.20 (t, $J$ = 7.5 Hz, 2 H, $-CH_2I$), 3.21 (s, 3 H, $-OCH_3$), 4.85 (br s, 1 H, $-CH[OC(CH_2)_2(OCH_3)]-$), 5.38 (s, 1 H, =CH–); MS (*m/e*, relative intensity) 306 (6), 249 (12), 121 (6), 97 (10), 83 (100); HRMS calcd for $C_{12}H_{19}OI$ (M − $HOCH_3$): 306.1890, found (M − $HOCH_3$) 306.0495.

***tert*-Butyl 3-[4-[3-(1-Methoxy-1-methylethoxy)-1-cyclopenten-1-yl]butyl]-2-oxocyclopentanecarboxylate, 10.** To a 0 °C suspension of NaH (0.014 g, 0.34 mmol) in THF (1 mL)

(10) (a) Wolff, S.; Schreiber, W. L.; Smith, A. B., III; Agosta, W. C. *J. Am. Chem. Soc.* **1972**, *94*, 7797. (b) Byrne, B.; Wilson, C. A., II; Wolff, S.; Agosta, W. C. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1550. (c) Herz, W.; Iyer, V. S.; Nair, M. G.; Saltiel, J. *J. Am. Chem. Soc.* **1977**, *99*, 2704. (d) Ayral-Kaloustian, S.; Wolff, S.; Agosta, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 5954. (e) Paquette, L. A.; Pansegrau, P.; Wiedeman, P.; Springer, J. *J. Org. Chem.* **1988**, *53*, 1461.

(11) Winkler, J.; Hong, B.; Bahador, A.; Kazanietz, M.; Blumberg, P. *Bioorg. Med. Chem. Lett.*, in press.

(12) Amouroux, R. *Heterocycles* **1984**, *22*, 1489.

was added *tert*-butyl 2-oxocyclopentanecarboxylate[13] (0.058 g, 0.31 mmol) in THF (0.5 mL) dropwise. After 10 min at 0 °C, the resulting mixture was treated with *n*-butyllithium (0.13 mL, 0.33 mmol), added dropwise. After an additional 10 min at 0 °C, the reaction mixture was treated with iodide **9** (0.116 g, 0.34 mmol) in THF (0.5 mL). After an additional 15 min at 0 °C, the reaction mixture was quenched by dropwise addition of methanol. When hydrogen evolution had ceased, the reaction mixture was diluted with saturated aqueous $NH_4Cl$ and extracted twice with diethyl ether. The combined organic layers were successively washed with water and saturated aqueous $NaHCO_3$, dried ($K_2CO_3$), and concentrated under reduced pressure. Flash chromatography of the crude residue (10% ethyl acetate/petroleum ether) gave the desired β-keto ester **10** (0.03 g, 72%): IR ($CDCl_3$) 2937, 1746, 1717, 1370, 1254, 1147 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.70 (m, 2 H), 1.36 (s, 6 H, $-OC(CH_3)_2-$), 1.47, 1.48 (s, 9 H, diastereomeric $-C(CH_3)_3$), 1.76 (m, 3 H), 2.01–2.30 (m, 10 H), 2.37 (m, 2 H), 3.02, 3.14 (m, 1 H, diastereomeric, $-CH(CO)(CO_2$-*t*-Bu)), 3.22 (s, 3 H, $-OCH_3$), 4.84 (br s, 1 H, $-CH[OC(CH_2)_2(OCH_3)]-$), 5.34 (s, 1 H, =CH–); MS (*m/e*, relative intensity) 248 (11), 230 (72), 213 (7), 202 (6), 185 (20), 165 (9), 151 (6), 119 (40), 105 (19), 93 (59), 80 (100); HRMS calcd for $C_{15}H_{20}O_3Si$ (M – O-t-Bu – $C(CH_3)_2OCH_3$) 248.3243, found (M – O-t-Bu – $C(CH_3)_2OCH_3$) 248.1425.

***tert*-Butyl 3-[4-(3-Oxo-1-cyclopenten-1-yl)butyl]-2-oxocyclopentanecarboxylate, 11.** To a solution of **10** (0.47 g, 1.23 mmol) in THF (1 mL) at 0 °C was added 100 μL of water and pyridinium *p*-toluenesulfonate (0.02 g, 0.12 mmol). After being stirred for 30 min at 0 °C, the reaction mixture was quenched with saturated aqueous $Na_2CO_3$ and extracted three times with diethyl ether. The combined organic layers were dried over $K_2CO_3$ and concentrated under reduced pressure. Flash chromatography of the crude residue (33% ethyl acetate/petroleum ether) gave the deprotected allylic alcohol (0.25 g, 65%): IR ($CDCl_3$) 3602, 2936, 1748, 1715, 1370, 1157 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.35 (m, 3 H), 1.47, 1.48 (s, 9 H, diastereomeric $-C(CH_3)_3$), 1.75 (m, 3 H), 2.03–2.35 (m, 9 H), 2.42 (m, 2 H), 3.02, 3.14 (m, 1 H, diastereomeric $-CH(CO)(CO_2$-t-Bu)), 4.8 (br s, 1 H, –CH(OH)–), 5.45 (s, 1 H, =CH–); MS (*m/e*, relative intensity) 313 (6), 286 (8), 248 (43), 230 (75), 202 (18), 185 (25), 154 (27), 137 (13), 119 (60), 105 (19), 93 (59), 80 (100); HRMS calcd for $C_{15}H_{20}O_3$ (M – HO-t-Bu) 248.3243, found (M – HO-t-Bu) 248.1413.

To a solution of the above allylic alcohol (0.02 g, 0.07 mmol) in $CH_2Cl_2$ (1 mL) at 25 °C was added pyridinium dichromate (0.040 g, 0.11 mmol). The reaction was stirred at 25 °C for 2 h and then diluted with diethyl ether. Elution of the organic solution through a silica gel column with diethyl ether gave enone **11** (0.02 g, 86%): IR ($CDCl_3$) 2936, 1705, 1676, 1615, 1369, 1257, 1153 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.42 (m, 5 H), 1.47, 1.48 (s, 9 H, diastereomeric $-C(CH_3)_3$), 1.61 (m, 3 H), 1.80 (m, 1 H), 2.05–2.31 (m, 2 H), 2.41 (m, 4 H), 2.57 (m, 2 H, $-CH_2(CO)-$), 3.02, 3.15 (m, 1 H, diastereomeric $-CH(CO)(CO_2$-t-Bu)), 5.91 (s, 1 H, =CH–); MS (*m/e*, relative intensity) 264 (15), 247 (23), 236 (5), 220 (13), 151 (7), 137 (17), 122 (16), 109 (100).

**Dioxenone 6.** To a solution of β-keto ester **11** (0.15 g, 0.48 mmol) in acetone (2.39 mL) at –78 °C was added trifluoroacetic anhydride (0.12 mL, 0.86 mmol) and trifluoroacetic acid (2.9 mL). The reaction was warmed to 25 °C over 18 h and then diluted with diethyl ether and slowly poured into a mixture of saturated aqueous $NaHCO_3$ and ice. The solution was intermittently checked with pH paper during this process to ensure that it was at all times slightly basic. The two layers were then separated, and the aqueous phase was extracted two times with diethyl ether. The combined ethereal extracts were dried (MgSO4) and concentrated under reduced pressure. Flash chromatography of the crude residue (50% ethyl acetate/petroleum ether) gave pure dioxenone **6** (0.075 g, 52%): IR ($CDCl_3$) 2933, 1713, 1676, 1643, 1615, 1422, 1259, 1199 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.41 (m, 3 H), 1.61 (m, 3 H), 1.70 (s, 3 H, $-OC(CH_3)(OR)-$), 1.71 (s, 3 H, $-OC(CH_3)(OR)-$), 2.18 (m, 1 H), 2.42 (m, 5 H), 2.52 (m, 1 H), 2.59 (m, 3 H), 2.78 (br s, 1 H), 5.94 (s, 1 H, =CH–); MS (*m/e*, relative intensity) 246 (6), 220 (12), 149 (8), 137 (13), 123 (13), 109 (100); UV ($CH_3CN$) 259.0 nm (ε = 8910 $cm^{-1}$ $M^{-1}$), 225.2 (ε = 16 600).

**Photoadducts 12 and 13.** A solution of dioxenone **6** (0.05 g, 0.18 mmol) in acetonitrile (100 mL) was degassed (by bubbling nitrogen through the solution for 1 h) and irradiated (450-W Hanovia lamp, Pyrex filter) at 0 °C for 4 h. Concentration of the solution under reduced pressure gave an inseparable mixture of diastereomeric photoadducts: IR ($CDCl_3$) 2933, 2867, 1723, 1639, 1416, 1260, 1200, 1150 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): δ 1.00–2.70 (m, 34 H), 1.54 (s, 3 H, $-C(CH_3)-$), 1.63 (s, 3 H, $-C(CH_3)-$), 1.68 (s, 3 H, $-C(CH_3)-$), 1.79 (s, 3 H, $-C(CH_3)-$); MS (*m/e*, relative intensity) 246 (100), 218 (34), 191 (6), 164 (5), 149 (6), 136 (11), 123 (16), 110 (23); UV ($CH_3CN$) 262.1 nm (ε = 6450 $cm^{-1}$ $M^{-1}$).

**Diketo Esters 14 and 15.** A solution of isomeric photoadducts **12/13** (0.11 g, 0.36 mmol) and *p*-toluenesulfonic acid monohydrate (0.014 g, 0.07 mmol) in methanol (10 mL) was heated to reflux for 18 h. Water (1 mL) was then added, and the solution was refluxed for an additional 30 min. Upon cooling to 25 °C, the solvent was removed under reduced pressure. The residue was diluted with diethyl ether and extracted twice with saturated aqueous $NaHCO_3$. The organic phase was dried ($K_2CO_3$) and concentrated under reduced pressure. The two isomeric diketo esters, **14** (0.04 g, 38%) and **15** (0.03 g, 26%), respectively, were obtained in a 1.4:1 ratio and were separated by flash chromatography (15% ethyl acetate/petroleum ether). Crystals suitable for X-ray analysis were obtained from the separated products by crystallization from ethyl acetate at –20 °C. **14**: mp 99.1–102.3 °C; IR ($CDCl_3$) 2932, 1728 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.30–2.37 (m, 14 H), 2.61 (d, *J* = 12.6 Hz, 1 H, $-CH(CO)-$), 3.54 (t, *J* = 10.0 Hz, 1 H, $-CH(CO)(CO_2Me)$), 3.76 (s, 3 H, $-CO_2CH_3$). **15**: mp 98.6–100.1 °C; IR ($CDCl_3$) 2928, 1728 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.15–2.61 (m, 15 H), 3.40 (t, *J* = 10.0 Hz, 1 H, $-CH(CO)(CO_2Me)$), 3.71 (s, 3 H).

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**Supplementary Material Available:** Tables of atomic coordinates, ORTEP plots, bond lengths and angles, and anisotropic thermal parameters for the X-ray crystal structures of diketo esters **14** and **15** and $^1H$ NMR spectra for all new compounds (**6–15**) (25 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(13) Banerjee, D.; Mahapatra, S. *Tetrahedron* **1960**, *11*, 234.