1,10-diaza-18-crown-6 (0.062 g, 0.2 mmol), and sodium carbonate (0.055 g, 0.6 mmol) was refluxed in dry acetonitrile (35 mL) for 2 h under argon. The reaction mixture was allowed to cool, the resulting suspension was filtered, and the filtrate was evaporated. Column chromatography (chloroform–ethanol 95:5) of the residue afforded **61**·NaBr·$2H_2O$ (63%) as a colorless gummy material: IR (KBr) 3455, 2880, 1630, 1545, 1390, 1360, 1100, 945 cm^{-1}; MS, *m/z* (relative abundance) 520 (3.1, M^+), 459 (2.5), 446 (6.5), 445 (21.2), 261 (10.7), 260 (19.1), 259 (28.2), 246 (21.6), 232 (9.4), 231 (10.3), 216 (21.2), 172 (21.0), 158 (13.7), 157 (10.1), 145 (11.6), 132 (16.1), 131 (100), 130 (19.9), 102 (17.1), 77 (10.4); ^1H NMR ($CDCl_3$) δ 9.48 (s, 2 H, H-3 and -3′), 7.87 (m, 2 H, H-4 and -4′), 7.26 (m, 2 H, H-6 and -6′), 7.12 (m, 2 H, H-5 and -5′), 3.95 (s, 4 H, $ArCH_2N$), 3.60 (m, 12 H, OCH_2CH_2O), 3.25 (m, 4 H, OCH_2CH_2O), 2.70 (m, 8 H, CH_2N). Anal. Calcd for $C_{28}H_{36}N_6O_4NaBr·2H_2O$: C, 50.99; H, 6.07; N, 12.75; Br, 12.11. Found: C, 50.98; H, 6.00; N, 12.69; Br, 12.25.

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Registry No. **2**, 61063-05-6; **4**, 61063-13-6; **8**, 113302-64-0; **9**, 113302-65-1; **10**, 16714-26-4; **11**, 113302-66-2; **12**, 113302-67-3; **13**, 113302-68-4; **14**, 113302-69-5; **15**, 113302-70-8; **16**, 113302-71-9; **17**, 113302-72-0; **18**, 113302-73-1; **19**, 113302-74-2; **20**, 113302-75-3; **21**, 113302-76-4; **22**, 113302-77-5; **23**, 113302-78-6; **24**, 113302-79-7; **25**, 113302-80-0; **26**, 33334-12-2; **27**, 66620-31-3; **28**, 113302-82-2; **29**, 20864-49-7; **30**, 34897-84-2; **31**, 57772-50-6; **32**, 113302-83-3; **33**, 113302-84-4; **34**, 80866-76-8; **35**, 5858-27-5; **36**, 84902-24-9; **37**, 113302-85-5; **38**, 113302-86-6; **42**, 113302-87-7; **43**, 3176-62-3; **44**, 113302-88-8; **45**, 113302-89-9; **46**, 113302-90-2; **47**, 113321-69-0; **48**, 113302-91-3; **49**, 113321-70-3; **50**, 113302-92-4; **51**, 113302-93-5; **52**, 113302-94-6; **53**, 113302-95-7; **54**, 113302-96-8; **55**, 113302-97-9; **56**, 113302-98-0; **57**, 113302-99-1; **58**, 113303-00-7; **58**·(NaSCN), 113275-00-6; **58**·(KSCN), 113275-02-8; **58**·($HgCl_2$), 113275-03-9; **58**·($PdCl_2$), 113275-04-0; **59**, 113303-01-8; **59**·(NaSCN), 113303-05-2; **59**-(KSCN), 113275-07-3; **60**, 113303-02-9; **60**·(NaSCN), 113275-09-5; **60**·(KSCN), 113275-11-9; **61**, 113303-03-0; **61**·(NaBr), 113275-05-1; 2-hydroxy-5-methylbenzaldehyde, 613-84-3; 2-methoxyethanol tosylate, 17178-10-8; tetraethyleneglycol ditosylate, 37860-51-8; tetraethyleneglycol, 112-60-7; 1,10-diaza-18-crown-6, 23978-55-4.

Conjugate Addition of Methanol to α-Enones: Photochemistry and Stereochemical Details

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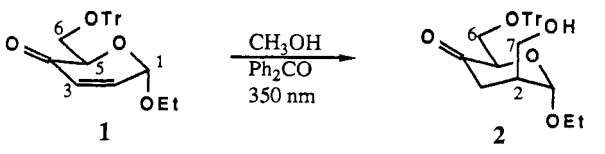
Previous studies seemed to indicate that the benzophenone-initiated photoaddition of methanol to the carbohydrate-derived α-enone **1** occurred more readily than to comparable carbocyclic α-enones. A mechanistic study was therefore undertaken (a) to establish the mechanistic details of the photoaddition reaction and (b) to compare the quantum yields of the carbohydrate and carbocyclic substrates. Evidence is presented that shows that the only important photochemical event is hydrogen abstraction (to give $^{\bullet}CH_2OH$) and that energy transfer to the enone substrate is not a factor. The course of addition of $^{\bullet}CH_2OH$ to **1** has been monitored by ESR spectroscopy, and the spectrum is best interpreted as involving the initial formation of an equilibrium mixture of the pseudochair and pseudoboat intermediates **26** and **27**, respectively. The quantum yields were determined for **1**, **5**, and **11** in order to discover the effect of (a) the pendant oxygen (**1** vs **5**) and (b) the ring oxygen (**5** vs **11**). The latter two give both axial and equatorial photoadducts, and within experimental error, there was no detectable difference in their reactivities. However, for the axial adduct formation, the carbohydrate enone **1** was found to be more reactive than oxane **5** or carbocycle **11**.

Introduction

In 1972, Fraser-Reid and co-workers reported that the carbohydrate-derived α-enone **1** undergoes efficient benzophenone-initiated photoaddition of methanol to give the hydroxymethyl adduct **2** (Scheme I).[2] In subsequent studies aimed at extending the scope of this process,[3,4] two general observations were made. Firstly, a wide variety of other oxygenated compounds of the type RCH_2OH, $RCH(OR')_2$, and RCHO also served as excellent addends.

Scheme I



1 **2**

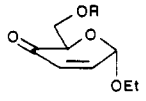
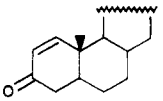
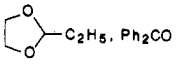
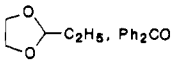
Secondly, the α-enone **1** appeared to react faster and give better yields than its carbocyclic counterparts. A sampling of the data relating to the latter observation is shown in Table I.

In subsequent years, the Fraser-Reid group has also observed unusual reactivity for enone **1**, as compared with other α-enones, in a variety of cycloaddition reactions.[5]

(1) Taken in part from the Ph.D. Thesis of Z.B., University of Maryland, 1986.
(2) Fraser-Reid, B.; Holder, N. L.; Yunker, M. B. *J. Chem. Soc., Chem. Commun.* **1972**, 1286.
(3) Fraser-Reid, B.; Holder, N. L.; Hicks, D. R.; Walker, D. L. *Can. J. Chem.* **1977**, *55*, 3978.
(4) Fraser-Reid, B.; Anderson, R. C.; Hicks, D. R.; Walker, D. L. *Can. J. Chem.* **1977**, *55*, 3986.
(5) For convenient summaries of these reactions, see: Fraser-Reid, B. *Acc. Chem. Res.* **1975**, *8*, 192; **1985**, *18*, 347.

0022-3263/88/1953-2066$01.50/0

Table I. Conjugate Addition Photoalkylation[a]

substrate	reagents	time, h	yield, %	ref
 1, R = Tr 1a, R = Ac	CH_3OH, Ph_2CO	8.5	75–90	3
2-cyclohexenone	CH_3OH, Ph_2CO	24, incomplete	33	3
1	CH_3CHO, Ph_2CO	5	67	4
	CH_3CHO, Ph_2CO	12	42	4
1		2	62	4
2-cyclohexenone		57	54	4

[a] All irradiations were conducted at 350 nm, with enone and benzophenone concentrations in the range of 0.2–1.0 M at 25 °C, using a Rayonet photochemical reactor (Model RPR-100).

These collective results imply that the reactivity of the α,β-unsaturated ketonic moiety is affected by the presence of oxygen(s) in the ring and/or pendant to it.

Semiempirical calculations (MNDO) lent weight to the implications, since it was found that the LUMO energies of α,β-unsaturated ketones could cover a wide spectrum, depending upon the placement of oxygen atoms.[6] It is desirable to determine to what extent these theoretical calculations can be correlated with experimental observations. Accordingly, it was deemed opportune to gain a better understanding of the results from the photoreaction of the enones shown in Table I, which served as the basis for our impression that 1 possessed enhanced reactivity. In addition, we wish to gain information about the mechanism for these photoadditions.

Three α-enones (1, 5, and 11) were chosen for the initial photochemical studies. Comparison of photoreaction with 1 and 5 would reveal the importance of the pendant oxygen (i.e., OEt) on the reactivity of the system, while comparison of 5 and 11 would relate to the effect of the ring oxygen.

Experimental Section

General Procedures. Melting points were determined in capillary tubes by using a Büchi Model 510 melting point apparatus and are uncorrected. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ. IR spectra were recorded on a Perkin-Elmer Model 297 instrument by using sodium chloride plates for thin films of liquids, syrups, or solids in CH_2Cl_2 solutions. Optical rotations were determined at the sodium D line by using a Perkin-Elmer 241 polarimeter with concentrations of 0.5–1.5 g/100 mL in $CHCl_3$. ^1H NMR spectra were determined on a Varian XL-300 spectrometer in $CDCl_3$ with residual $CHCl_3$ as the standard. The progress of all reactions was monitored by thin-layer chromatography (TLC), which was performed on aluminum plates precoated with silica gel HF-254 (0.2-mm layers) containing a fluorescent indicator (Merck, 5539). Detection was first by UV (254 nm), then charring with sulfuric acid spray, or charring with a solution of ammonium molybdate(VI) tetrahydrate (12.5 g), and cerium(IV) sulfate tetrahydrate (5.0 g) in 10% aqueous sulfuric acid (500 mL). Flash chromatograhy was performed by using Kieselgel 60 (230–400 mesh, Merck).

Preparation of Compound 4c. In a round-bottomed flask, "triacetyl glucal" 3 (2.74 g, 10 mmol) was dissolved in dry dichloromethane (25 mL), cooled to 0 °C under argon, and then $BF_3{\cdot}Et_2O$ (2.47 mL, 0.2 equiv) was added, followed by triethylsilane (1.91 mL, 1.2 equiv). Stirring was continued at 0 °C under argon until the reaction was complete (TLC, ~2–3 h). The mixture was poured into ice water and stirred for ~30 min. The organic layer was separated and washed with saturated sodium bicarbonate solution, dried (Na_2SO_4), and processed in the usual way. Chromatography afforded compound **4a** (1.83 g, 85%), which was dissolved in 75 mL of methanol/water/triethylamine (5:4:1 ratio) and stirred at room temperature until the reaction was complete (TLC). The solvents were evaporated, and column chromatography of the syrup using 5% EtOH in 1:1 petroleum ether/ethyl acetate afforded **4b** (1.1 g, 97%). To a solution of the diol **4b** (1.0 g, 7.70 mmol) in the minimum amount of dry pyridine were added chlorotriphenylmethane (3.21 g, 11.5 mmol) and a catalytic amount of 4-(dimethylamino)pyridine. The flask was equipped with a drying tube, and its contents were stirred until the reaction was shown to be complete by TLC (~24 h). The mixture was diluted with water and extracted with ether. The organic layer was concentrated in vacuo and the residue azeotroped with toluene to remove traces of pyridine. The crude syrup was then purified by flash column chromatography (20% ethyl acetate in petroleum ether) on silica gel. The product **4c** was a white crystalline solid (2.01 g, 70%): mp 130–132 °C; TLC R_f 0.33 (30% ethyl acetate in petroleum ether); $[\alpha]^{25}_D$ −41.7°; IR (CH_2Cl_2) 3500 (OH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.65 (d, 1, $J_{3,OH}$ = 3.3 Hz, C3-OH), 3.30 (td, 1, $J_{2,3}$ = $J_{2,7'}$ = 8.7 Hz, $J_{2,7}$ = 3.6 Hz, H2), 3.51 (m, 2 ,H7), 4.15 (m, 3, H3, 2 H6), 5.82 (m, 2, H4, H5), 7.30 (m, 15, triphenylmethyl).

Anal. Calcd for $C_{25}H_{24}O_3$: C, 80.62; H, 6.50. Found: C, 80.63; H, 6.73.

Preparation of α-Enone 5. A solution of alcohol **4c** (1.00 g, 2.7 mmol) in dry methylene chloride (50 mL) was treated with a mixture of sodium acetate (900 mg, 11 mmol) pyridinium chlorochromate (2.35 g, 11 mmol), Celite (1.0 g), and Florisil (150 mg) at 0 °C. The mixture was stirred at room temperature under anhydrous conditions, and upon completion (TLC, ~2 h), the mixture was diluted with half the volume of ether. The mixture was filtered through a sintered-glass funnel containing silica gel, and the filter cake was washed with ether until TLC indicated that all the product was collected. The solution was concentrated in vacuo and purified further by flash chromatography (petroleum ether/ethyl acetate, 4:1) to yield a white crystalline solid **5** (547 mg, 55%): mp 124–126 °C; TLC R_f 0.34 (20% ethyl acetate in petroleum ether); $[\alpha]^{25}_D$ −11.2°; IR (CH_2Cl_2) 1690 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.56 (m, 2, 2 H7), 4.27 (m, 1, H2), 4.44 (br d, 1, H6), 4.63 (ddd, 1, $J_{5,6'}$ = 4.2 Hz, $J_{4,6'}$ = 1.8 Hz, $J_{6,6'}$ = 18.6 Hz, H6′), 6.22 (dt, 1, $J_{6,4}$ = 1.8 Hz, $J_{5,4}$ = 9.5 Hz, H4), 7.15 (dt, 1, $J_{6,5}$ = 4.2 Hz, H5), 7.35 (m, 15, triphenylmethyl).

Anal. Calcd for $C_{25}H_{22}O_3$: C, 81.06; H, 5.99. Found: C, 81.26; H, 6.02.

Preparation of Ketones 7a and 8. (a) The enone **5** (200 mg, 0.541 mmol) was subjected to standard preparative photoreaction conditions (see below) for photoreaction with methanol. After a primary purification of the products by flash chromatography (20% ethyl acetate in petroleum ether), in which both products eluted together, the solution was concentrated in vacuo and the products were separated by preparative HPLC (isocratic: methylene chloride/2-propanol/petroleum ether, 31:4:65), the fraction containing a clear syrup **7a** (53 mg, 24%) and a white amorphous solid **8** (42 mg, 19%). Compound **7a** existed in a 1.6:1 ratio with its hemiketal form **6**. Compound **7a** showed the following characteristics: TLC R_f 0.20 methylene chloride/2-propanol/petroleum ether, 8:1:11; $[\alpha]^{25}_D$ +25.8°; IR (CH_2Cl_2) 3400 (OH), 1730 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.82 (m, 1, C8-OH), 2.34 (m, 1, H5), 2.62 (d, 2, $J_{4,5}$ = 4.8 Hz, H4), 3.46 (m, 2, H7), 3.78 (m, 2, H8), 3.87 (dd, 1, $J_{5,6}$ = 3.0 Hz, $J_{6,6'}$ = 12.0 Hz, H6), 3.95 (dd, 1, $J_{2,7}$ = 3.9 Hz, $J_{2,7'}$ = 6.0 Hz, H2), 4.20 (dd, 1, $J_{5,6'}$ = 4.2 Hz, H6′), 7.35 (m, 15, triphenylmethyl).

Anal. Calcd for $C_{26}H_{26}O_4$: C, 77.59; H, 6.51. Found: C, 77.42; H, 6.58.

(b) The chloroacetate **7b** (21 mg, 0.044 mmol) was dissolved in 0.5 mL of a 5:1 mixture of dry pyridine and dry ethanol. To this solution was added 5 mg (0.6 equiv) of thiourea. A drying tube was added and the mixture stirred at 100 °C for 20 min. TLC showed deprotection and decomposition. The pyridine was removed under high vacuum with a dry-ice trap, and the residue

(6) Fraser-Reid, B.; Underwood, R.; Osterhout, M.; Grossman, J. A.; Liotta, D. *J. Org. Chem.* **1986**, *51*, 2152.

was purified by flash column chromatography on silica gel (20–30% ethyl acetate/petroleum ether). Evaporation of solvent left a clear syrup **7a** (4 mg, 23%) whose NMR spectrum was identical with that of the material described in part a.

Compound **8** showed the following characteristics: TLC R_f 0.15 (methylene chloride/2-propanol/petroleum ether, 8:1:11); $[\alpha]^{25}_D$ +41.8°; IR (CH_2Cl_2) 3400 (OH), 1730 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.54 (br s, 1, C8-OH), 2.38 (dd, 1, $J_{4a,4e}$ = 15.6 Hz, $J_{4a,5}$ = 8.7 Hz, H4a), 2.56 (m, 1, H5), 2.73 (dd, 1, $J_{4e,5}$ = 6.9 Hz, H4e), 3.40 (dd, 1, $J_{2,7}$ = 4.1 Hz, $J_{7,7'}$ = 9.1 Hz, H7), 3.49 (dd, 1, $J_{2,7'}$ = 2.6 Hz, H7'), 3.63 (m, 3, H6, 2 H8), 3.96 (dd, 1, H2), 4.32 (dd, 1, $J_{6,6'}$ = 11.7 Hz, $J_{5,6'}$ = 3.9 Hz, H6'), 7.35 (m, 15, triphenylmethyl).

Anal. Calcd for $C_{26}H_{26}O_4$: C, 77.59; H, 6.51. Found: C, 77.42; H, 6.58.

Preparation of Ketone 7b. The mixture of **7a** and **6** (18 mg, 0.045 mmol) was dissolved in dry pyridine (1 mL) and cooled to 0 °C. This solution was treated with chloroacetic anhydride (17 mg, 0.1 mmol). TLC showed that the reaction was complete within a few minutes. Pyridine was removed under high vacuum with a dry-ice trap and the residue purified by flash chromatography on silica gel (10% ethyl acetate in petroleum ether). Compound **7b** was obtained as a clear syrup (21 mg, 98%): TLC R_f 0.11 (20% ethyl acetate in petroleum ether); $[\alpha]^{25}_D$ +42.9°; IR (CH_2Cl_2), 1740, 1770 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.60 (m, 3, H5, 2 H4), 3.44 (dd, 1, $J_{2,7}$ = 4.8 Hz, $J_{7,7'}$ = 10.3 Hz, H7), 3.52 (dd, 1, $J_{2,7'}$ = 3.0 Hz, H7'), 3.87 (dd, 1, $J_{5,6}$ = 3.9 Hz, $J_{6,6'}$ = 12.1 Hz, H6), 4.01 (dd, 1, H2), 4.06 (s, 2, H9), 4.12 ($J_{6',5}$ = 7.8 Hz, H6'), 4.35 (d, 2, $J_{8,8'}$ = 6.9 Hz, H8), 7.35 (m, 15, triphenylmethyl).

Anal. Calcd for $C_{28}H_{26}O_5Cl$: C, 70.21; H, 5.68. Found: C, 70.04; H, 5.50.

***syn*-6-[(Triphenylmethoxy)methyl]-2-cyclohexen-1-ol (10b).** *cis*-6-(Hydroxymethyl)-2-cyclohexen-1-ol (**10a**) was prepared from the ester **9** according to the procedure of Bailey and co-workers.[9] A portion of the material (210 mg, 1.64 mmol) was tritylated, as described above for the analogue **4b**. After purification by flash chromatography (10% ethyl acetate in petroleum ether), the solution was concentrated in vacuo to yield a clear syrup **10b** (364 mg, 60%): TLC R_f 0.50 (20% ethyl acetate in petroleum ether); IR (CH_2Cl_2) 3300 (OH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.20–1.50 (m, 3, 2 H5, H6), 1.85–2.20 (m, 3, H1, 2 H4), 3.18 (t, 1, $J_{6,7}$ = $J_{7,7'}$ = 6.0 Hz, H7), 3.28 (dd, 1, $J_{6,7'}$ = 4.0 Hz, H7'), 4.40 (br s, 1, C1-OH), 5.90 (s, 2, H2, H3), 7.45 (m, 15, triphenylmethyl).

Anal. Calcd for $C_{26}H_{26}O_2$: C, 84.29; H, 7.07. Found: C, 84.39; H, 7.25.

6-[(Triphenylmethoxy)methyl]-2-cyclohexenone (11). The allylic alcohol **10b** (364 mg, 0.984 mmol) was oxidized with pyridinium chlorochromate, as described for **5**. After purification by flash chromatography on silica gel (5% ethyl acetate in petroleum ether), the solution was concentrated in vacuo to yield the white crystalline solid **11** (344 mg, 95%): mp 110–111 °C; TLC R_f 0.33 (20% ethyl acetate in petroleum ether); IR (CH_2Cl_2) 1670 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.95 (m, 1, H5), 2.35 (m, 3, 2 H4, H5'), 2.60 (m, 1, H6), 3.30 (t, 1, $J_{6,7}$ = $J_{7,7'}$ = 9.0 Hz, H7), 3.50 (dd, 1, $J_{6,7'}$ = 3.8 Hz, H7'), 6.00 (d, 1, $J_{2,3}$ = 9.8 Hz, H2), 6.98 (m, 1, H3), 7.40 (m, 15, triphenylmethyl).

Anal. Calcd for $C_{26}H_{24}O_2$: C, 84.75; H, 6.57. Found: C, 84.79; H, 6.52.

***cis*-2-[(Triphenylmethoxy)methyl]-5-(hydroxymethyl)-cyclohexanone (12) and *trans*-2-[(Triphenylmethoxy)-methyl]-5-(hydroxymethyl)cyclohexanone (13).** The enone **11** (204 mg, 0.554 mmol) was subjected to standard preparative photoreaction conditions (see below) with methanol. After purification by flash chromatography (20% ethyl acetate in petroleum ether), the products were separated by preparative HPLC (isocratic:methylene chloride/2-propanol/petroleum ether, 31:4:65). The solution of each product was concentrated in vacuo to yield **12** as a clear syrup (59 mg, 27%) and **13** as a white crystalline solid (47 mg, 21%). The axial adduct **12** displayed the following properties: TLC R_f 0.21 (methylene chloride/2-propanol/petroleum ether, 8:1:11); IR (CH_2Cl_2) 3400 (OH), 1705 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.50 (br s, 1, C8-OH), 1.62 (m, 1, H4), 1.78 (m, 2, H3, H4'), 2.05 (m, 1, H3'), 2.16 (m, 2, H5, H6a), 2.38 (t, 1, $J_{5,6e}$ = $J_{6a,6e}$ = 8.1 Hz, H6e), 2.70 (m, 1, H2), 3.21 (dd, 1, $J_{2,7}$ = 7.2 Hz, $J_{7,7'}$ = 9.3 Hz, H7), 3.40 (dd, 1, $J_{2,7'}$ = 7.5 Hz, H7'), 3.45 (m, 2, H8), 7.30 (m, 15, triphenylmethyl).

Anal. Calcd for $C_{27}H_{28}O_3$: C, 80.97; H, 7.05. Found: C, 80.86; H, 6.97.

The equatorial adduct **13** displayed the following properties: mp 188–190 °C; TLC R_f 0.18 (methylene chloride/2-propanol/petroleum ether, 8:1:11); IR (CH_2Cl_2) 3400 (OH), 1700 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.50 (m, 3, H3, 2 H4), 1.98 (m, 2, H3', H5), 2.14 (t, 1, $J_{5,6a}$ = $J_{6a,6e}$ = 13.2 Hz, H6a), 2.40 (ddd, 1, $J_{4,6e}$ = 1.8 Hz, $J_{5,6e}$ = 3.9 Hz, H6e), 2.54 (m, 2, H2, C8-OH), 3.11 (dd, 1, $J_{2,7}$ = 7.8 Hz, $J_{7,7'}$ = 8.7 Hz, H7), 3.55 (m, 3, H7', 2 H8), 7.30 (m, 15, triphenylmethyl).

Anal. Calcd for $C_{27}H_{28}O_3$: C, 80.97; H, 7.05. Found: C, 81.00; H, 6.93.

Table II. Retention Times of Components in the Direct Quantum Yield Experiments for the Reaction 1 → 2[a]

major component	t_R, min	minor component	t_R, min
Ph_2CO	3.5	$(Ph_2COH)_2$	6.5
1	5.6	$Ph_2C(OH)CH_2OH$	14.1
4c[b]	11.2	Ph_3COH	4.6
2	18.8		

[a] The solvent was a mixture of *tert*-butyl methyl ether and hexane, mixing being programmed so that the percentages of the former were as follows: 0 min (10); 5 min (20); and 20 min (100). The flow rate was 1 mL/min, and UV detection was at 270 nm. [b] Internal standard.

Standard Procedure for Preparative Photoreactions. A solution of the enone (2.2×10^{-2} M) and benzophenone (0.15 equiv) was prepared in HPLC grade methanol in a Pyrex tube, which was placed 10 cm from a water-cooled immersion well containing a 450-W Hanovia mercury lamp and Pyrex filter. A long syringe needle was used to bubble argon through the solution during the irradiation. The reaction was monitored by TLC and was usually complete in approximately 15 min. On occasion, benzophenone would be consumed during the reaction and it was necessary to add more. When the starting enone had disappeared, the photolysate was concentrated in vacuo and the residue purified by flash chromatography on silica gel. Continued irradiation after disappearance of the starting enone resulted in formation of two pinacol byproducts resulting from benzophenone–methanol reactions.

HPLC Analytical Procedures. General. High-performance liquid chromatography (HPLC) was carried out on a Varian 5000 instrument. Two solvent reservoirs were used with automatic mixing. A Varian UV-100 variable-wavelength microprocessor-controlled ultraviolet absorbance detector was used.

Direct Quantum Yield Experiments. For these analyses, a CN-5 Micropak column (15 cm long, packed with 5-μm particles) was used. The details are given in Table II.

Relative Quantum Yield Experiments. For these analyses, reverse-phase analysis was carried out on a Micropak MCH-5 N_{cap} column, 15 cm long and packed with 5-μm particles. The details are given in Table III.

Quantum Yield (Absolute) for Reactions 1 → 2. Quantum yield measurements for product **2** formation from benzophenone-induced photoreactions of **1** in methanol were made by using a "linear-optical-bench" apparatus, which has been previously described.[13] Light of wavelength 300–350 cm was used for the irradiations. This was obtained by use of a three-compartment

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Scheme II

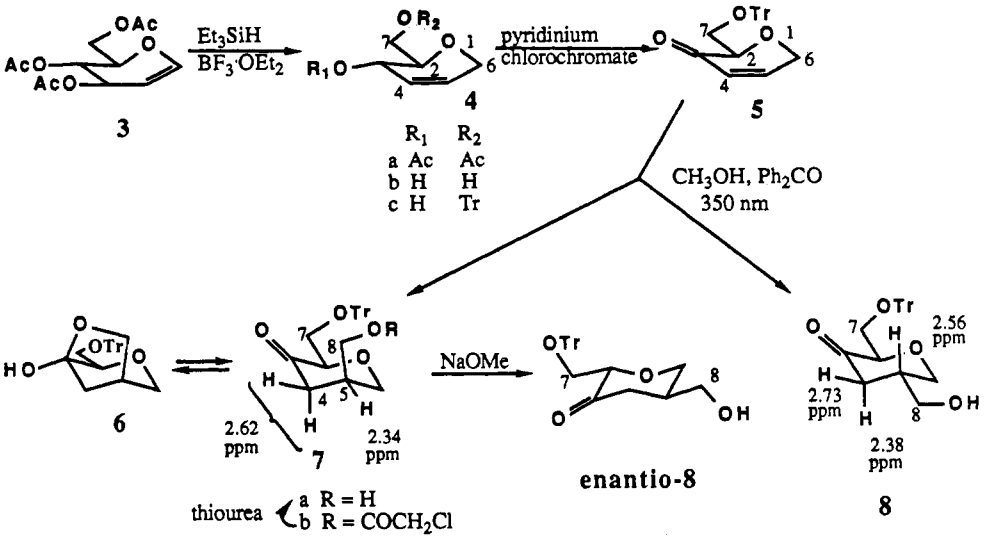


Table III. Retention Times of Compounds in the Relative Quantum Yield Experiments

substrate	solvent[a]	major component[b]	t_R, min
1	A	Ph_2CO	4.8
		2	11.7
		5[c]	15.1
		1	21.0
11	A	Ph_2CO	4.0
		12	8.4
		13	9.5
		5[c]	13.4
		11	20.2
5	B	Ph_2CO	4.8
		7a	8.8
		8	9.4
		5	16.0
		11[d]	23.0

[a] Solvent A was a mixture of acetonitrile and water, mixing being programmed so that the percentages of the former were as follows: 0 min (50); 15 min (50); 20 min (75); 23 min (75); and 24 min (50). The flow rate was 2 mL/min. Solvent B was a mixture of acetonitrile and methanol (1:1) and water, where the percentages of the 1:1 mixture to water were as follows: 0 min (60); 10 min (60); 15 min (70); 20 min (70); 21 min (80); and 25 min (80). The flow rate was 1.5 mL/min. [d] Minor components having the approximate retention times shown were also identified: $Ph_2C(OH)CH_2OH$ (~1.5 min); Ph_3COH (~7.0 min); $(Ph_2COH)_2$ (~13.0 min). UV detection was at 270 nm. [c] Internal standard for substrates 1 and 11. [d] Internal standard for substrate 5.

filter solution cell filled with 2.0 M $NiSO_4$ in 5% H_2SO_4, 0.8 M $CoSO_4$ in 5% H_2SO_4, and 0.0133 M $SnCl_2$ in 40% HCl.

Solutions of enone 1 (39.2×10^{-6} mol) and benzophenone (98.0×10^{-6} mol) in 50 mL of methanol were irradiated for time periods required to bring about the conversion to product 2, as listed in Table IV. The photolysates were transferred quantitatively to a round-bottomed flask, and an aliquot of the stock solution of 4c (containing 21.5×10^{-6} mol) was added as an internal calibration standard. Trial experiments had shown that 4c was suitable for quantitative analytical HPLC measurements using a UV detector. Peak areas in the chromatogram were determined by the "cut and weigh" procedure, appropriate corrections being applied on the basis of previously determined "response factors" for the calibration standard 4c. Light absorbed by benzophenone was measured by use of a calibrated photocell system.[13] The quantum yield results are recorded in Table IV.

Relative Quantum Yields for Formation of 7a, 8, 12, and 13. Quantum yields for formation of adducts 7a, 8, 12, and 13 were determined by use of a carousel apparatus and employing the photoreaction 1 → 2 as the actinometer. Independent solutions of enones 1, 5, and 11 (each at 32.0×10^{-6} mol) and benzophenone (16.0×10^{-6} mol) in 20 mL of methanol in quartz vessels were purged with argon and then irradiated simultaneously with an apparatus consisting of a Hanovia 450-W lamp surrounded by a Pyrex filter. The irradiations were conducted four times for time periods of 12, 13, 14, and 15 min. In each case, the photolysates were individually transferred to a round-bottomed flask and an aliquot of the stock solution of the following materials was added to serve as HPLC calibration standard. For *substrates* 1 and 11, the reference material was enone 5 (8.9×10^{-6} mol); for *substrate* 5, the HPLC reference material was enone 11 (10.2×10^{-6} mol). Light absorbed by benzophenone in each solution was determined by use of the amount of product 2 formed from enone 1 and the known (see above) quantum yield for this process. The quantum yield data obtained from this experiment are summarized in Table V.

Results and Discussion

Synthesis of Substrates and Characterization of Products. Enone 1 and the adduct 2 obtained from it have been described previously.[3] Enones 5 and 11 were prepared by the standard transformations summarized in Schemes II and III, respectively (see Experimental Section for details). Assignment of structures to the photoproducts 12 and 13 was based on the ^1H NMR parameters shown in Scheme III for H5, H6a, and H6e, these having been identified by decoupling experiments. Thus, the H5 signals at 2.16 and 1.98 ppm are indicative of 12 and 13, respec-

Table IV. Determination of Quantum Yields for Formation of 2 from Enone 1[a]

entry	conversion, %	light output[b] ($\times 10^{-6}$ E)	2, moles ($\times 10^{-6}$)	material balance[c]	quantum yield (Φ)	
i	15.4	46.37	6.07	101	0.131	
ii	13.4	37.61	5.24	98	0.139	av = 0.139 ± 0.008 (5.8%)
iii	12.1	32.35	4.75	98	0.147	

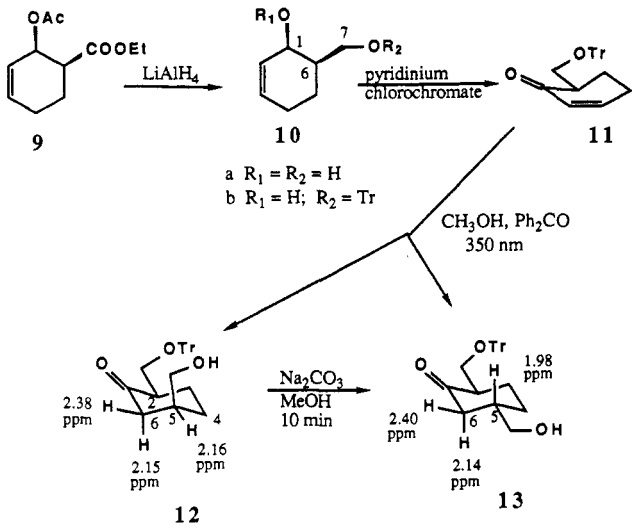
[a] Each experiment contained 39.2×10^{-6} mol of 1 and 97.9×10^{-6} mol of Ph_2CO in 50 mL of solution in MeOH. [b] These values were determined after calibration of the system by ferrioxalate actinometry.[11,12] The light was filtered through three cells containing the following solutions:[10] (1) 2.0 M $NiSO_4$ in 5% H_2SO_4; (2) 0.8 M $CoSO_4$ in 5% H_2SO_4; (3) 0.0133 M $SnCl_2$ in 40% HCl. [c] This is expressed as a percentage of 1 initially present and represents the amount of unreacted 1 and 2 produced.

Table V. Relative Quantum Yields from "Carousel" Experiments

expt	substrate (moles × 10^{-6})	irradn time, min	% conversion[a]	material balance,[b] %	quantum yield[c]		
i	**5** (32.0)	15	15.3	95.0	0.118		
ii	**5** (32.0)	13	12.5	91.9	0.110		
iii	**5** (32.0)	12	12.3	99.1	0.121	0.116 ± 0.007 (6.0%)	**7a**, axial
iv	**5** (32.0)	14	14.9	95.9	0.116		
i	**5** (32.0)	15	8.47		0.066		
ii	**5** (32.0)	13	6.91		0.061		
iii	**5** (32.0)	12	6.81		0.067	0.064 ± 0.004 (5.8%)	**8**, equatorial
iv	**5** (32.0)	14	8.25		0.064		
i	**11** (32.1)	15	14.2	97.4	0.111		
ii	**11** (32.1)	13	11.9	94.1	0.105		
iii	**11** (32.1)	12	11.5	92.1	0.114	0.109 ± 0.005 (4.6%)	**12**, axial
iv	**11** (32.1)	14	13.4	94.4	0.104		
i	**11** (32.1)	15	7.76		0.060		
ii	**11** (32.1)	13	6.45		0.057		
iii	**11** (32.1)	12	6.42		0.064	0.060 ± 0.004 (6.8%)	**13**, equatorial
iv	**11** (32.1)	14	7.35		0.057		

[a] Expressed as a percentage of the indicated product to the initial enone substrate. [b] This is expressed as a percentage of the enone substrate initially present and represents unreacted enone and products. In the case of **5** and **11**, the total of products **7a** + **8** and **12** + **13** for each of the experiments i–iv was used for the calculation. [c] These values were calculated as (moles of product × Φ_2)/moles of **2**. Φ_2 was determined as 0.139 in Table IV.

Scheme III



tively, by virtue of the normal chemical shift differences between chemically similar axial and equatorial protons.[7] Support for these structural assignments came from the fact that treatment of **12** with sodium carbonate in methanol for 10 min caused quantitative formation of the other primary photoproduct **13**. Notably, treatment of **13** with base had no effect on the molecule.

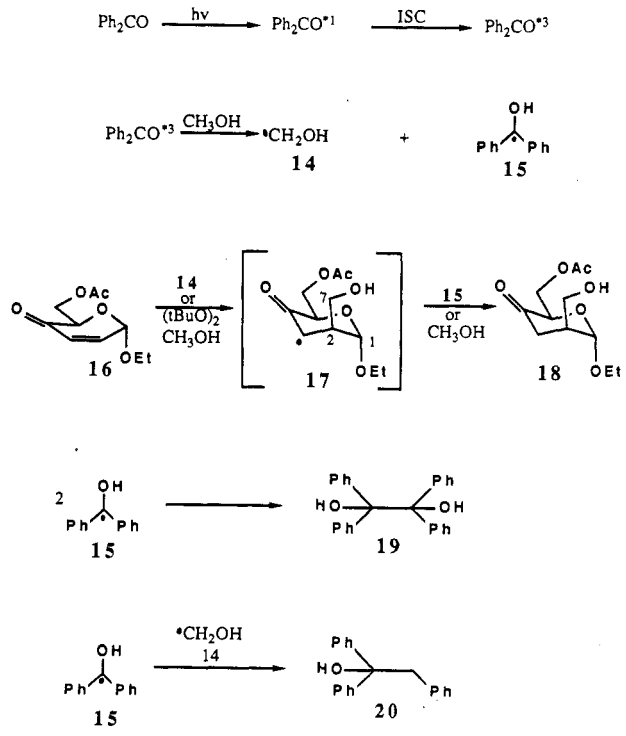
Similarly, base equilibration of **7a** (Scheme II) for 10 min led to the formation of *enantio*-**8**, whereas base had no effect on **8** over the same time period. The photoadduct **7a** was found to be in equilibrium with its cyclic ketal form, a derivative that is not possible for **8**. The existence of the equilibrium was confirmed when a mixture of **7a** and **6** was found to give **7b** only upon chloroacetylation. Subsequent removal of the ester with thiourea[8] regenerated the original mixture of **7a** and **6**.

Mechanism for Adduct Formation. The UV parameters for key α-enones are shown in Table VI. The benzophenone-photoinduced addition reactions occurring between conjugated enones and methanol are believed to proceed via the mechanistic pathway outlined in Scheme IV. In this process, the triplet excited state of benzophenone, formed by excitation and efficient intersystem crossing, abstracts a hydrogen atom from methanol to form the hydroxymethyl **14** and ketyl **15** radicals. Studies by Topp[14] have shown that hydrogen atom abstraction from

Table VI. UV Spectral Data of Selected Enones

compound	λ_{max}, nm	ϵ, M^{-1}
16	207	3.39×10^3 π-π^*
	269	3.77×10^2 n-π^*
1	199	6.09×10^4
	232	8.40×10^3
	258	7.00×10^2 n-π^*
5	198	5.21×10^4
	232	1.12×10^4
	257	2.07×10^3 n-π^*

Scheme IV



methanol by benzophenone triplets is fast ($k = 3.8 \times 10^6$ s^{-1} in MeOH at 293 K). Alternative routes involving energy transfer from benzophenone (E_T = 69 kcal/mol) to the enone, followed by α-hydrogen atom abstraction by the triplet enone, appear unlikely on the bases of a number of earlier observations. For example, the triplet states of

(14) Topp, M. R. *Chem. Phys. Lett.* **1975**, *32*, 144.

conjugated enones lie at energies greater than 70 kcal/mol.[15a] Thus, energy transfer in these systems should be inefficient, especially in light of the large rates for benzophenone triplet hydrogen atom abstraction.[16,17]

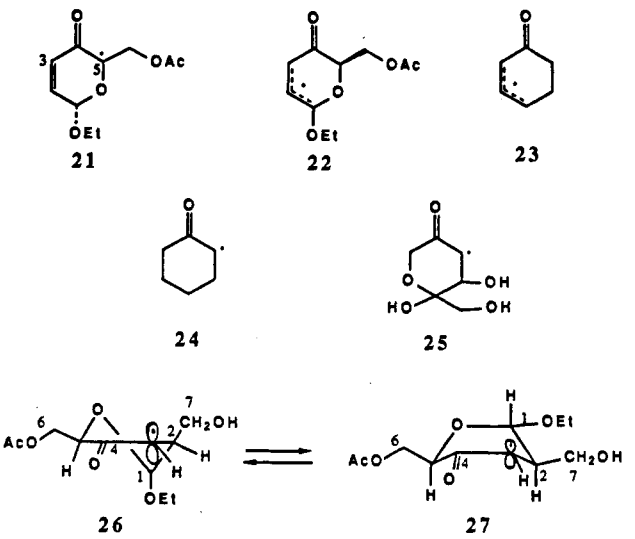
Observations made during studies employing *p*-methoxyacetophenone lend further support to these conclusions. This aryl ketone has a π-π^* triplet of energy (E_T = 71.5 kcal/mol) greater than that of benzophenone. Yang and co-workers[18] have demonstrated that the quantum yield for *p*-methoxyacetophenone photoreduction in isopropyl alcohol is low (Φ = 0.04 compared to 0.68 for acetophenone), owing to the inability of π-π^* ketone triplets to participate in H-atom abstraction processes. *Importantly, irradiation of methanol solutions of p-methoxyacetophenone containing the enone 1 failed to result in formation of methanol adduct 2.* This result serves as strong evidence in favor of the mechanism presented in Scheme IV.[19]

Conjugate addition of the hydroxymethyl radicals to enone **16** (Scheme IV) results in generation of the enone radical **17**. This addition process[20,21] should be favored by the nucleophilic nature of radical **14**. Importantly, similar routes have been employed to rationalize enone quenching of benzophenone photoreduction[15a] and solvent additions to enones.[15b] Addition of **14** to ground-state enones should occur in competition with coupling to form pinacols (e.g., **19** and **20**).[22,23] Finally, hydrogen atom transfer to **17** from the ketyl radical **15** or methanol results in production of the adducts.

ESR Studies. In order to gain a better understanding of the stereochemical aspects of $^{\bullet}CH_2OH$ addition, we studied the reaction by ESR techniques. However, because of solubility problems, the acetylated enone **16** was used instead of the tritylated counterpart **1**. The stereochemical course of addition to both is known to be the same.[2-4] Irradiation of mixtures containing benzophenone gave rise to a very strong signal for **15**, which blocked out all other signals. However, irradiation of a mixture of di-*tert*-butyl peroxide and methanol in methylcyclohexane at 263 K gave a good signal for **14** [a_1 = 17.42 G (CH_2), a_2 = 1.47 G (OH)]. When enone **16** was added to this mixture, the hydroxymethyl radical signal disappeared and was replaced by a new signal consisting of a broad doublet of doublets, a_1 = 21.2 G, a_2 = 18.1 G; g = 2.0042. If the irradiation was continued for a few minutes, the doublet of doublets disappeared and the signal due to **14** reappeared. This seemed to coincide with the disappearance of the starting enone.

The unidentified new radical could have arisen either by hydrogen abstraction from the enone (in which case the enone must be a better hydrogen donor than methanol) or by addition of the hydroxymethyl radical to the enone to give **17**. As a check on the first possibility, a dilute solution of enone **16** in di-*tert*-butyl peroxide was irradiated in the ESR cavity. A good signal was detected comprising two overlapping spectra: (a) a set of 16 sharp lines, tentatively assigned to radical **21** (Scheme V) with a_1 = 0.73 G (H3), a_2 = 3.26 G (H1), a_3 = 8.40 G (H6), a_4 = 9.87 G (H6′); and (b) a set of eight broad lines, tentatively assigned to radical **22** with a_1 = 1.6 G (H5), a_2 = 3.2 G (H2), a_3 = 14.9 G (H3). For comparison, a solution of cyclohexenone in di-*tert*-butyl peroxide was similarly irradiated. It gave a good spectrum, which could be reasonably assigned to the radical **23**, generated by hydrogen atom abstraction from the allylic CH_2 group, and could be analyzed as follows: a_1 (2 H) = 0.99 G (H6), a_2 (1 H) = 2.80 G (H3), a_3 (2 H) = 3.07 G (H5), a_4 (2 H) = 15.89 G (H2 and H4).

Scheme V



In light of these results, it is reasonable to ascribe the broad doublet of doublets detected when enone **16** was irradiated in methanol/di-*tert*-butyl peroxide to a radical formed by addition of hydroxymethyl radical to the enone system. In an attempt to obtain further structural information, we generated the adduct radical at lower temperatures. Unfortunately, the signal remained as a broad doublet of doublets and no fine structure could be resolved. However, it was noted that the hyperfine splitting constants were temperature dependent, e.g., at 233 K, a_1 = 19.5 G and a_2 = 17.8 G, while at 180 K, a_1 = 19.0 G and $a_2 \cong$ 17.5 G. The greater temperature dependence indicates that a_1 arises from coupling of the free spin with a β-proton, while the fact that it *decreases* in magnitude with *decrease* in temperature indicates that the average value of $\cos^2\theta$, where θ is the dihedral angle between the SOMO orbital and C_β–H bond, also decreases with temperature.[24]

The most likely structure, **17**, for the adduct radical is consistent with the observed stereochemistry of the photoproduct (**18**) and with the expectation that approach of the $^{\bullet}CH_2OH$ radical to the enone system in **16** will be sterically directed to the face anti to the axial ethoxy substituent. Unfortunately, there are few relevant ESR data available in the literature. The radical **24**, generated from cyclohexanone, has a (α-H) = 18.1 G,[25] in good agreement with the value observed for **17**. Also, it is

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(16) Loutfy and de Mayo[17] have shown that $k_q = 6.1 \times 10^5$ M s^{-1} for cyclopentenone (E_T = 73 kcal/mol) quenching of benzophenone triplets. Thus, the rates of energy transfer when enone concentrations are ca. 1 mM would be ca. 6×10^2 as compared to 3.3×10^6 for H-atom abstraction.

(17) Loutfy, R. O.; de Mayo, P. *J. Chem. Soc., Chem. Commun.* **1970**, 1040.

(18) Yang, N. C.; McClure, D. S.; Murov, S. L.; Houser, J. J.; Dusenbury, R. *J. Am. Chem. Soc.* **1967**, *89*, 5468.

(19) Also, irradiation of methanol solutions of **1** with Pyrex-filtered light under identical conditions used in the benzophenone-induced processes did not lead to generation of adduct **2**.

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(21) Goth, H.; Cerutti, P.; Schmid, H. *Helv. Chim. Acta* **1965**, *48*, 1395.

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(24) Ayscough, P. B. *Electron Spin Resonance in Chemistry*; Methuen: London, 1967; pp 77–78.

(25) Gilbert, R. C.; Norman, R. O. C.; Sealy, R. C. *J. Chem. Soc., Perkin Trans. 2* **1973**, 2174.

Table VII. Summary of Quantum Yield Data

enone	quantum yield for adduct formation
1	(2) 0.139 ± 0.008
5	(7a) 0.116 ± 0.007
	(8) 0.064 ± 0.004
11	(12) 0.109 ± 0.005
	(13) 0.060 ± 0.004

known[26] that substituted cyclohexyl radicals generally give hyperfine splitting constants of about 40 G for axial β-protons and about 10 G for equatorial β-protons. The radical **25**, in which the β-H is probably axial, has a (α-H) = 18.0 G and a (β-H) = 36.0 G.[27]

For the radical **17**, the magnitude of the β-hyperfine splitting constant precludes a conformation in which the β-proton is strictly equatorial. On the other hand, it is unlikely that interconversion of two pseudochair forms of **17** would occur rapidly enough to give a time-averaged spectrum at the temperatures used here. However, the salient features of the spectrum, viz., the broadness of the peaks and the temperature dependence of hyperfine splitting, are consistent with fast equilibrium between pseudochair (**26**) and pseudoboat (**27**) forms in which the radical center is approximately planar, and overlap is maintained between the SOMO orbital and the carbonyl π system. Since $\cos^2 \theta$ is smaller in **26** than **27**, the observed temperature dependence indicates that **26** is the more stable.

Quantum Yields and Stereochemistry. On the basis of the mechanism presented in Scheme IV, the relative quantum yields for adduct formation under identical conditions (i.e., equivalent enone concentrations) should depend upon partitioning of the hydroxymethyl radical via conjugate addition vs pinacolization. Thus, efficiencies for adduct formation should reflect the reactivity of the enones with the nucleophilic radical **14**. As the data in Table VII indicate, there is no detectable difference between the reactivities of enones **5** and **11** as studied. Thus, the results suggest that the ring oxygen, by itself, does not play a significant role in governing the rates of conjugate addition by the hydroxymethyl radical.

The hydroxymethyl radical addition to enone **1** displays a high degree of axial stereoselectivity. In this case, the axial hydroxymethyl adduct **2** is formed exclusively. In contrast, benzophenone-induced photoadditions to the enone **5** and **11** show only a slight (ca. 2:1) preference for formation of the axial adducts. It should be noted that photoadduct formation in the case of enone **11** (and most probably for **5** as well) is under kinetic control. Thus, no epimerization is detected when either **12** or **13** in pure form is subjected to the photoreaction conditions.

These results suggest that the stereochemical course of hydroxymethyl radical additions to these enones is under both steric and stereoelectronic control, with the former factor being of primary importance. Accordingly, axial addition to C2 in **1** is strictly enforced by the presence of the axial ethoxy group at C1. When this substituent is absent, as in **5** and **11**, a more modest axial selectivity is seen, likely resulting from maintenance of greater orbital overlap in the developing enol radical.

Summary

This study was prompted by the observation that $^{\bullet}CH_2OH$ appeared to react faster and gave better chemical yields with carbohydrate α-enones than with carbocyclic substrates. The quantum yield studies show that, for axial adduct formation, the carbohydrate enone **1** was found to be more active than enone **5** or **11**. However, within experimental error, there was no detectable difference between the reactivities of **5** and enone **11**. The implication, therefore, is that the role of the ring oxygen in these photoreactions is not significant. The ESR studies show that the benzophenone-sensitized addition reaction involves conjugate 1,4-addition of $^{\bullet}CH_2OH$ to the enone **16**.

Acknowledgment. We thank Martha Brumfield and Alicia Bowser for their assistance. We acknowledge financial support provided by NSF (CHE 8304283) and NIH (GM 27251).

Registry No. **1**, 113429-24-6; **3**, 2873-29-2; **4a**, 52945-57-0; **4b**, 52945-60-5; **4c**, 113353-22-3; **5**, 113353-23-4; **6**, 113378-68-0; **7a**, 113353-24-5; **7b**, 113353-26-7; **8**, 113353-25-6; *enantio*-**8**, 113531-16-1; **9**, 113353-27-8; **10a**, 33073-68-6; **10b**, 113353-28-9; **11**, 113353-29-0; **12**, 113353-30-3; **13**, 113353-31-4; methanol, 67-56-1.

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