

Stereoselective [2+2] Photocycloaddition of Chiral 2(5*H*)-furanones to Alkenes

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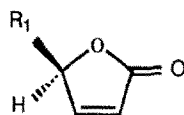
Dedicated to Prof. Kurt Schaffner in his 60th birthday.

Abstract: The steric and stereoelectronic dependence of the diastereoselectivity in the photochemical [2+2] cycloaddition of chiral 2(5*H*)-furanones to alkenes is investigated to prepare eventually cyclobutanic natural products. It is shown that the alkenes approach to different chiral 5-substituted 2(5*H*)-furanones mainly by the less hindered side.

INTRODUCTION

Conveniently substituted cyclobutane rings are present in some natural products: spatane diterpenes,¹ bourbene² and caryophyllene³ sesquiterpenes, (+)-grandisol monoterpene,⁴ etc. To generate such rings in the total synthesis of some of these substances, 2(5*H*)-furanones have been successfully used via a [2+2] photocycloaddition to alkenes.⁵ The photochemical behaviour of these α,β -butenolides has been widely studied,⁶ but the stereoselective control (mainly face diastereoselectivity) of their cycloaddition to olefines has not received so much attention.⁵ If a certain control for this cycloaddition could exist and the 2(5*H*)-furanone is homochiral the reactions would lead to good diastereomeric excesses and ultimately to enantiomerically pure natural products. In fact, this approach has been widely used through thermal cycloadditions and Michael additions.^{7,8} We can imagine that steric and stereoelectronic effects can force the olefine to approach the furanone through its less hindered side thus creating a diastereofacial differentiation. To clarify the extend of these effects we have prepared some optically pure 5-alkyl-2(5*H*)-

furanones, **1-5**, and we have followed the diastereoselective course of their photochemical [2+2] cycloaddition to tetramethylethylene (TME) and ethylene.

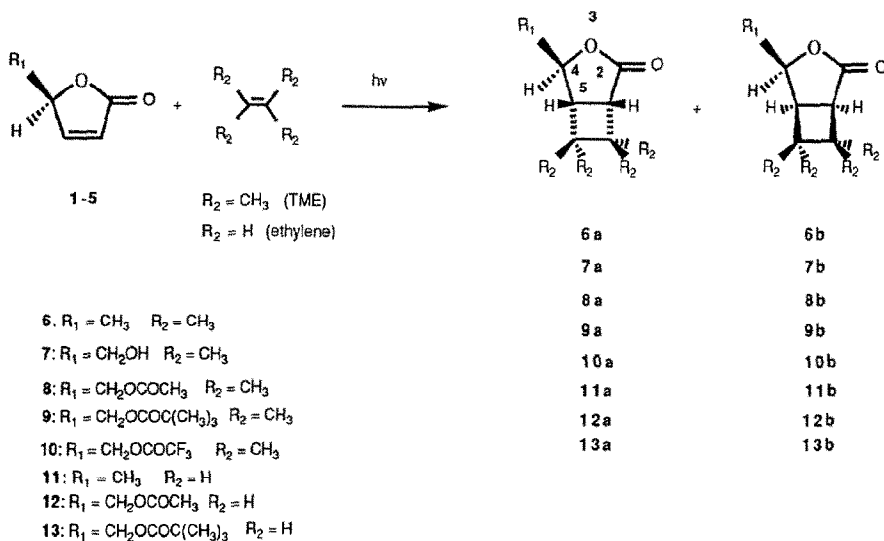


- 1:** $R_1 = \text{CH}_3$
2: $R_1 = \text{CH}_2\text{OH}$
3: $R_1 = \text{CH}_2\text{OCOCH}_3$
4: $R_1 = \text{CH}_2\text{OCOC}(\text{CH}_3)_3$
5: $R_1 = \text{CH}_2\text{OCOCF}_3$

RESULTS and DISCUSSION

Cycloaddition of **1** to TME afforded two cycloadducts, **6a** and **6b** in a ratio 73:27 according to glc analysis (TABLE I). Both diastereoisomers were separated by column chromatography.

SCHEME I



The relative configuration of these isomers was determined by the coupling constant of H_4 ($\delta = 4.6$ ppm and $\delta = 3.8$ ppm in the major and minor cycloadduct respectively) with H_5 ($\delta = 2.34$ ppm and $\delta = 1.70$

ppm in the major and minor cycloadduct) measured in their 400 MHz ^1NMR spectra. The major adduct showed $J_{4,5} = 1.5$ Hz and was assigned to an *exo* (**6a**) relationship between R_1 and the cyclobutane ring while the minor one showed $J_{4,5} = 5.6$ Hz and was assigned to the *endo* isomer (**6b**).

furanone	R_1	olefine	d. e. %	yield % a+b	cycloadduct ratio a:b
1	CH ₃	TME	46	37	73:27
2	CH ₂ OH	TME	48	42	74:26
3	CH ₂ OCOCH ₃	TME	56	40	78:22
4	CH ₂ OCOC(CH ₃) ₃	TME	64	44	82:18
5	CH ₂ OCOCF ₃	TME	60	20	80:20
1	CH ₃	ethylene	18	48	59:41
3	CH ₂ OCOCH ₃	ethylene	48	46	74:26
4	CH ₂ OCOC(CH ₃) ₃	ethylene	56	49	78:22

TABLE I: Dependence of the cycloadduct ratio on the substituents in the γ -position of the chiral furanone and the olefine.

Furanones **2-5** gave with TME adducts **7a,7b-10a,10b**, and similarly furanones **1, 3** and **4** (see scheme I) gave with ethylene adducts **11a,11b-13a,13b**. NMR data used to assign the stereochemistry of the adducts are given in TABLE II. The major cycloadduct had always the smallest $J_{4,5}$ and was assigned as the *exo* diastereoisomer (**a**). In all cases adducts were separated by column chromatography and isolated with the exception of the trifluoroacetate derivatives that showed very sensitive to hydrolysis.

Table I shows the variation of the a/b cycloadduct ratio in function of R_1 found by glc analysis. For TME this ratio increases from 73:27 when $R_1 = \text{CH}_3$ to 82:18 when R_1 is the bulky $\text{CH}_2\text{OCOC}(\text{CH}_3)_3$. That fact denotes some kind of interactions between R_1 and the olefine. These interactions are still present when the olefine is the small ethylene molecule: a/b passes from 59:41 to 78:22 for $R_1 = \text{CH}_3$ and $\text{CH}_2\text{OCOC}(\text{CH}_3)_3$ respectively. For this olefine the diastereoisomeric excesses are not so large as for TME: only 18% when $R_1 = \text{CH}_3$ and 56% when $R_1 = \text{CH}_2\text{OCOC}(\text{CH}_3)_3$. Steric interactions can be immediately invoked to justify these facial diastereoselectivities, the β -side of the butenolide being hindered by R_1 . However, attention should be paid that do not exist big differences in the a/b ratios although these differences increase gradually with the size of the group linked to the furanone, from the small CH_3 to the bulky pivaloate moiety. That suggests that although the steric effect does really operate in spite of the bulky group being attached far away of the reactive double bond, probably a stereoelectronic effect is also present.

cycloadduct	H ₄		H ₅		J _{4,5}	
	δ, multiplicity		δ, multiplicity		Hz	
	a	b	a	b	a	b
6	4.6, dq	3.8, dq	2.34, dd	1.70, dd	1.5	5.6
7	4.5, ddd	4.6, m	2.65, dd	2.83, dd	1.2	5.0
8	4.6, ddd	4.6, ddd	2.49, dd	2.85, dd	1.5	5.7
9	4.6, ddd	4.6, ddd	2.45, dd	2.85, dd	1.9	5.8
10	4.8, ddd	4.7, ddd	2.50, dd	2.89, dd	1.7	6.0
11	4.5, dq	4.6, dq	3.2, m	3.15, m	1.0	5.7
12	4.55, ddd	4.60, ddd	2.95, m	3.25, m	1.0	5.6
13	4.59, ddd	4.62, ddd	2.96, m	3.2, m	1.2	5.2

TABLE II: Chemical shift, multiplicity and coupling constants for H₄ and H₅ in the cycloadducts.

Table I shows, also, that a/b is almost identical when TME reacts with furanone **1** or **2** ($R_1 = \text{CH}_2\text{OH}$) but changes when it reacts with furanone **3** where an ester group is present in R_1 . This group appears in furanones **3**, **4** and **5** that give cycloadducts **8**, **9** and **10** with the highest values of a/b. In these cases stereoelectronic effects, similar to the ones invoked in the alkylation of lithium butanolide enolates,⁹ that is the n- π interaction between the non-bonding electrons of oxygen with the π -orbitals of the butenolide (fig. 1), could induce a preferential α -attack (fig.2).

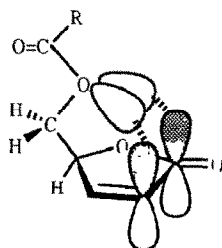


Figure 1

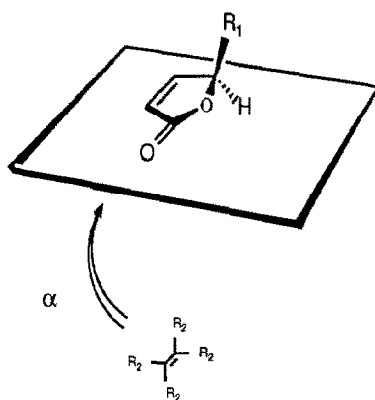


Figure 2

Therefore, steric and stereoelectronic effects operate in the photocycloaddition of homochiral 2(5H)-furanones to alkenes creating a diastereofacial differentiation that allows to obtain moderate diastereoisomeric excesses of the *exo* cycloadduct.

EXPERIMENTAL SECTION

Melting points were determined on a Kofler hot stage and are uncorrected. Optical rotations were obtained on a Propol polarimeter, Model Dr. Kerchen. Distillation of small amounts were effected on a rotational distillator, Büchi Model KRV 65/30 (only external or oven temperature given).

The 80 MHz pmr and 20 MHz cmr spectra were recorded on a Bruker spectrometer Model WP80SY and the 400 MHz pmr and 100 MHz cmr spectra were recorded on a Bruker AM400Wb, from chloroform-*d* solutions, unless otherwise indicated; chemical shifts are given in ppm relative to TMS (δ scale). Uv and ir spectra were recorded on a Hewlett-Packard 8452A and a Nicolet 20X spectrophotometers respectively.

Gas chromatographic analyses were performed on a Hewlett-Packard model 5930 instrument with a capillary column Hewlett-Packard Ultra 1 (crosslinked methyl silicone gum, 12m x 0.2mm x 0.3 μ m). The 70 eV electron impact mass spectra were recorded with a Hewlett-Packard apparatus Model 5985 B. Gc-ms analyses (70 eV for electron impact) were recorded on a Hewlett-Packard 5989 A gc-ms system with the previously described capillary column. Microanalyses were performed at the Instituto de Química Bio-Orgánica C.S.I.C., Barcelona.

General experimental procedure for photocycloadditions of 2(5*H*)-furanones with TME and ethylene.

Irradiations were performed in a small conventional photochemical reactor, consisting of a two-necked 50 mL reaction vessel and a water-jacketed Pyrex immersion well, using a high pressure 125 W mercury lamp (Philips HPK-125), usually under an argon atmosphere and with magnetic stirring. Ethylene saturated solutions at -78 °C were used in the cycloaddition experiments of this olefine. Water was used for refrigeration of the immersion well jacket.

The photoreactor was cooled with a dry ice-acetone, dry-ice-carbon tetrachloride or a running water bath (for room temperature experiments). The progress of the reactions was generally monitored by glc or tlc taking aliquots of ca 50 µL.

Furanones **1** and **2**, **3** were prepared from *D*-ribonolactone¹⁰ and *D*-mannitol^{11,12} respectively.

(-)-(S)-5-Pivaloyloxymethyl-2(5*H*)-furanone, 4.

To an ice-cooled solution of **2** (3.20g, 28.07 mmol), anhyd pyridine (4.50 mL, 55.86 mmol) and 4-dimethylaminopyridine (DMAP) (0.75 g, 6.07 mmol) in 60 mL CH₂Cl₂, pivaloyl chloride (6.80 mL, 55.43 mmol) was added. The mixture was magnetically stirred at room temperature for 29 h. After addition of water (10 mL), the organic layer was washed successively with 5% HCl (3x25 mL), satd aq NaHCO₃ (3x25 mL) and water satd NaCl (3x25 mL), and dried over anhyd Na₂SO₄. The solvent was removed under reduced pressure and the crude was chromatographed through silica gel (1 : 2 ethyl acetate-hexane as eluent) to afford **4** (4.96 g, 89% yield) as a colorless needles; m.p. 32-34°C; b.p. 90°C/0.1 torr; $\{\alpha\}_D^{20}$ -140 (c 1.3, in chloroform); ir (KBr) 3088, 3056, 2976, 2928, 2864, 1758, 1730, 1616, 1484, 1330, 1284, 1172, 1157, 805 cm⁻¹; pmr (80 MHz) 1.1 (s, 9H, (CH₃)₃C), 4.4 (d, $J_{6,5}$: 4.0 Hz, 2H, H-6), 5.2 (m, 1H, H -5), 6.1 (dd, $J_{3,4}$: 5.6 Hz, $J_{3,5}$: 2.2 Hz, 1H, H-3), 7.42 (dd, $J_{4,3}$: 5.6 Hz, $J_{4,5}$: 1.6 Hz, 1H, H-4); cmr (20 MHz) 26.8, 38.6, 61.9, 80.8, 122.8, 152.4, 171.9, 177.6; ms, m/e 199 (M⁺+1, 0.1), 168 (0.4), 142 (1.0), 98 (8.5), 97 (12.0), 85 (21.6), 84 (73), 57 (100), 55 (10.8), 41 (31.6).

(-)-(S)-5-Trifluoroacetyloxymethyl-2(5*H*)-furanone, 5.

A mixture of **2** (319 mg, 2.79 mmol) and trifluoroacetic anhydride (4 mL, 28.32 mmol) was magnetically stirred for 6 h under argon atmosphere. The crude was distilled with four portions of carbon tetrachloride at reduced pressure to remove the excess of the anhydride and trifluoroacetic acid. The residue obtained was distilled to afford **5** (534 mg, 91% yield). The ester is extremely sensitive to hydrolysis. B.p. 85-90 °C/0.1 torr; $\{\alpha\}$ -96.8 (c 2.1 in chloroform); ir (film) 3100, 2950, 1789, 1763, 1625, 1160, 1348, 1225 cm⁻¹; pmr (80 MHz) 4.5 (dd, J_{gem} : 12.0 Hz, $J_{6a,5}$: 5.2 Hz, 1H, H-6a), 4.8 (dd,

J_{gem} : 12.0 Hz, $J_{6b,5}$: 2.7 Hz, 1H, H-6b), 5.3 (m, 1H, H-5), 6.3 (dd, $J_{3,4}$: 6.4 Hz, $J_{3,5}$: 2.7 Hz 1H, H-3), 7.5 (dd, $J_{4,3}$: 6.4 Hz, $J_{4,5}$: 1.8 Hz, 1H, H-4); cmr (20 MHz) 65.1, 80.2, 114 (q, $J_{C,F}$: 285 Hz), 123.2, 152.0, 157 (q, $J_{C,F}$: 44 Hz), 172; ms, m/e 181 ($M^+ + 1$ -30, 6), 180 (8), 153 (2), 99 (5), 96 (32), 84 (5), 83 (100), 69 (54), 55 (51), 54 (14), 42 (13).

(-)-(1*S*,4*R*,5*R*)-4-Methyl-6,6,7,7-tetramethyl-3-oxabicyclo[3.2.0]heptan-2-one, 6a and (1*R*,4*R*,5*S*)-4-Methyl-6,6,7,7-tetramethyl-3-oxabicyclo[3.2.0]heptan-2-one, 6b.

A solution of **1** (300 mg, 3.06 mmol) and tetramethyl ethylene (TME) (3.6 mL, 30.42 mmol) in dry ether (45 mL) was irradiated at room temperature for 2 h through quartz. Elimination of the solvent at reduced pressure gave a residue which was chromatographed on silica gel using initially hexane alone and then a mixture of hexane and ether, gradually increasing the amount of ether, as eluent (0→30% ether in hexane). The first fraction gave (-)-**6a** (150 mg, 27% yield) as colorless crystalline solid; m.p. 55-56°C; $\{\alpha\}_D$ -81.3 (c 2.1 in chloroform); ir (KBr) 2975, 2930, 2871, 1758, 1479, 1457, 1376, 1334, 1280, 1167, 1108, 951 cm^{-1} ; pmr (400 MHz) 1.02 (s, 3H), 1.05 (s, 6H), 1.20 (s, 3H), 1.27 (d, $J_{8,4}$: 6.5 Hz, 3H, H-8), 2.34 (dd, $J_{5,1}$: 8.1 Hz, $J_{5,4}$: 1.5 Hz, 1H, H-5), 2.70 (d, $J_{1,5}$: 8.1 Hz, 1H, H-1), 4.60 (dq, $J_{4,8}$: 6.5 Hz, $J_{4,5}$: 1.5 Hz, 1H, H-4); cmr (20 MHz) 20.4, 20.7, 22.1, 26.0, 26.9, 39.9, 40.8, 46.4, 47.9, 76.7, 177.9; ms, m/e 183 ($M^+ + 1$, 1.9), 182 (1.1), 167 (0.2), 139 (1.0), 123 (4.3), 99 (12.8), 84 (35.5), 83 (98.4), 69 (48.0), 67 (39.5), 55 (100), 41 (77). Anal. Calc. for $C_{11}H_{18}O_2$: C, 72.52; H, 9.90. Found: C, 72.60; H, 10.06.

The second fraction gave **6b** (37 mg, 10% yield) as a liquid that was unsuitable for optical rotation measurements; b.p. 105°C/0.02 torr; ir (film): 2974, 2877, 1764, 1480, 1455, 1382, 1279, 1189, 1163, 1130, 1042, 986, 951 cm^{-1} ; pmr (400 MHz) 1.0 (s, 3H), 1.05 (s, 3H), 1.18 (s, 3H), 1.20 (s, 3H), 1.50 (d, $J_{8,4}$: 7.4 Hz, 3H, H-8), 2.68 (complex absorption, 2H, H-1, H-5), 4.58 (m, $J_{8,4}$: 7.4 Hz, 1H, H-4); pmr (400 MHz) (toluen- d_8) 0.50 (s, 3H), 0.65 (s, 3H), 0.80 (s, 6H), 0.90 (d, $J_{8,4}$: 7.4 Hz, 3H, H-8), 1.70 (dd, $J_{5,1}$: 8.0 Hz, $J_{5,4}$: 5.6 Hz, 1H, H-5), 1.96 (d, $J_{1,5}$: 8.0 Hz, 1H, H-1), 3.80 (dq, $J_{4,8}$: 7.4 Hz, $J_{4,5}$: 5.6 Hz, 1H, H-4); cmr (20 MHz) 16.1, 20.1, 22.9, 26.5, 26.9, 40.8, 42.1, 46.8, 48.5, 79.2, 178.2; ms m/e ($C_{11}H_{18}O_2$) 183 ($M^+ + 1$, 5.8), 139 (1.5), 123 (6.1), 99 (6.6), 95 (9.6), 84 (33.9), 83 (91.2), 82 (11.4), 69 (42.6), 67 (34.3), 55 (65.9), 41 (100).

The third fraction gave (74 mg) of the unreacted lactone **1**.

(-)-(1*S*,4*S*,5*R*)-4-Hydroxymethyl-6,6,7,7-tetramethyl-3-oxabicyclo[3.2.0]heptan-2-one, 7a and (1*R*,4*S*,5*S*)-4-Hydroxymethyl-6,6,7,7-tetramethyl-3-oxabicyclo[3.2.0]heptan-2-one, 7b.

A solution of **2** (315 mg, 2.76 mmol) and TME (3.5 mL, 29.47 mmol) in dry ether (45 mL) was irradiated at 20°C for 3 h through quartz. The reaction was monitored by tlc. The solvent was removed at

reduced pressure and the residue was chromatographed on silica gel. Elution with hexane-ethyl acetate (3:1) afforded (-)**7a** (142 mg, 31% yield) as a colorless crystalline solid, **7b** (50 mg, 11% yield) as an oil that was unsuitable for optical rotation measurements, and 47 mg of unreacted lactone **2**. (-)**7a**: m.p. 92-94°C; $[\alpha]_D -71.75$ (c 1.24 in chloroform); ir (KBr) 3680-3408-3100 (broad band), 2976, 2865, 1734, 1482, 1457, 1376, 1346, 1277, 1224, 1189, 1158, 1054, 998 cm^{-1} ; pmr (80 MHz) 1.05 (s, 3H), 1.10 (s, 6H), 1.20 (s, 3H), 1.95 (broad, s, 1H, -OH), 2.65 (dd, $J_{5,1}$: 8.5 Hz, $J_{5,4}$: 1.2 Hz, 1H, H-5), 2.80 (d, $J_{1,5}$: 8.5 Hz, 1H, H-1), 3.6 (dd, J_{gem} : 12.2 Hz, $J_{8a,4}$: 3.6 Hz, 1H, H-8a), 3.80 (dd, J_{gem} : 12.2 Hz, $J_{8b,4}$: 4.9 Hz, 1H, H-8b), 4.50 (ddd, $J_{4,8b}$: 4.9 Hz, $J_{4,8a}$: 3.6 Hz, $J_{4,5}$: 1.2 Hz, 1H, H-4); cmr (20 MHz) 20.3, 20.6, 25.8, 26.7, 39.7, 41.2, 43.2, 47.0, 64.7, 80.8, 178.6; ms m/e 198 (M^+ , 0.2), 180 (0.2), 167 (3.7), 155 (1.2), 121 (1.6), 84 (9.5), 83 (100), 69 (17.3), 55 (30.1), 43 (27.3), 42 (41.2). Anal. Calc. for $\text{C}_{11}\text{H}_{18}\text{O}_3$: C, 66.64; H, 9.15. Found: C, 66.68; H, 9.22. **7b**: ir (film) 3730-3050 (broad), 2960, 2928, 2873, 1765, 1457, 1375, 1279, 1183, 1158, 1141, 1071, 1005, 984, 900 cm^{-1} ; pmr (400 MHz) 1.0 (s, 6H), 1.10 (s, 3H), 1.20 (s, 3H), 1.90 (broad, s, 1H, -OH), 2.75 (d, $J_{1,5}$: 8.3 Hz, 1H, H-1), 2.83 (dd, $J_{5,1}$: 8.3 Hz, $J_{5,4}$: 5.0 Hz, 1H, H-5), 3.75 (dd, J_{gem} : 12.4 Hz, $J_{8a,4}$: 2.5 Hz, 1H, H-8a), 4.25 (dd, J_{gem} : 12.4 Hz, $J_{8b,4}$: 8.3 Hz, 1H, H-8b), 4.60 (m, 1H, H-4); cmr (20 MHz) 20.2, 23.3, 26.2, 26.9, 40.8, 42.0, 44.4, 47.5, 62.2, 85.3, 177.7; ms m/e 199 (M^+ +1, 4.1), 181 (1.4), 167 (3.5), 115 (2.4), 84 (23.6), 83 (100), 73 (34.2), 69 (21.1), 57 (12.6), 55 (44.5), 45 (37.6), 41 (45.0).

(-)-(1S,4S,5R)-4-acetyloxymethyl-6,6,7,7-tetramethyl-3-oxabicyclo[3.2.0]heptan-2-one, **8a** and (1R,4S,5S)-4-acetyloxymethyl-6,6,7,7-tetramethyl-3-oxabicyclo[3.2.0]heptan-2-one, **8b**.

A solution of **3** (309 mg, 1.98 mmol) and TME (2.4 mL, 20.20 mmol) in dry ether (45 mL) was irradiated at -20 °C for 2 h through quartz. The solvent was eliminated under reduced pressure to afford a crude, which was chromatographed on silica gel (0→10% ethyl acetate in hexane). From the rapidly eluted fractions, (-)**8a** (146 mg, 31% yield) was obtained as a colorless oil; b.p. 120-125 °C/0.3 torr; $[\alpha]_D -37.1$ (c 0.66 in chloroform); ir (film) 2960, 1765, 1746, 1373, 1232, 1159; pmr (400 MHz) 1.0 (s, 3H), 1.06 (s, 6H), 1.20 (s, 3H), 2.07 (s, 3H), 2.49 (dd, $J_{5,1}$: 8.2 Hz, $J_{5,4}$: 1.5 Hz, 1H, H-5), 2.73 (d, $J_{1,5}$: 8.2 Hz, 1H, H-1), 4.04 (dd, J_{gem} : 11.9 Hz, $J_{8a,4}$: 4.6 Hz, 1H, H-8a), 4.18 (dd, J_{gem} : 11.9 Hz, $J_{8b,4}$: 3.6 Hz, 1H, H-8b), 4.65 (ddd, $J_{4,8a}$: 4.6 Hz, $J_{4,8b}$: 3.6 Hz, $J_{4,5}$: 1.5 Hz, 1H, H-4); cmr (20 MHz) 20.3, 20.5, 20.6, 25.8, 26.8, 40.0, 41.3, 43.6, 46.6, 65.9, 77.1, 170.3, 177.3; ms, m/e 181 (M^+ -59, 1), 167 (6), 152 (3), 99 (4), 84 (14), 83 (100), 69 (10), 43 (29). Anal. Calc. for $\text{C}_{13}\text{H}_{20}\text{O}_4$: C, 64.98; H, 8.39. Found: C, 64.81; H, 8.42.

From the slowly eluted fractions, **8b** (44 mg, 9% yield) was isolated as an oil that was unsuitable for optical rotation measurements; ir (film) 2959, 2928, 1768, 1744, 1373, 1234, 1179, 1159 cm^{-1} ; pmr (400 MHz) 1.0 (s, 6H), 1.02 (s, 3H), 1.20 (s, 3H), 2.10 (s, 3H), 2.70 (d, $J_{1,5}$: 7.7 Hz, 1H, H-1), 2.85 (dd, $J_{5,1}$: 7.7 Hz, $J_{5,4}$: 5.7 Hz, 1H, H-5), 4.31 (dd, J_{gem} : 12.2 Hz, $J_{8a,4}$: 3.0 Hz, 1H, H-8a), 4.49 (dd, J_{gem} : 12.2 Hz, $J_{8b,4}$: 8.2 Hz, 1H, H-8b), 4.61 (ddd, $J_{4,8}$: 8.2 Hz, $J_{4,5}$: 5.7 Hz, $J_{4,8a}$: 3.0 Hz, 1H, H-4); cmr (20 MHz)

20.1, 20.2, 20.4, 23.1, 26.1, 40.8, 41.9, 44.5, 47.1, 63.4, 80.8, 170.5, 177.0; ms, m/e 181 (M^+ -59, 1) 167 (4), 152 (2), 98 (3), 84 (23), 83 (100), 69 (15), 55 (10), 43 (23).

(-)-(1*S*,4*S*,5*R*)-4-pivaloyloxymethyl-6,6,7,7-tetramethyl-3-oxabicyclo[3.2.0]heptan-2-one, 9a and (1*R*,4*S*,5*S*)-4-pivaloyloxymethyl-6,6,7,7-tetramethyl-3-oxabicyclo[3.2.0]heptan-2-one, 9b.

A solution of **4** (212 mg, 1.07 mmol) and TME (1.5 mL, 12.63 mmol) in dry ether (45 mL) was irradiated at 20 °C for 3 h through quartz. The solvent was removed to give a crude that was chromatographed through silica gel (mixtures of hexane-ether as eluents). The first fraction gave **9b** (25 mg, 8% yield) that was unsuitable for optical rotation measurements; ir (film) 2960, 2924, 2854, 1773, 1734, 1452, 1380, 1356, 1260, 1140, 1116, 1020, 900 cm^{-1} ; pmr (400 MHz) 1.02 (s, 3H), 1.04 (s, 3H), 1.15 (s, 3H), 1.20 (s, 9H, $(\text{CH}_3)_3\text{C}$), 1.22 (s, 3H), 2.70 (d, $J_{1,5}$: 7.8 Hz, 1H, H-1), 2.88 (dd, $J_{5,1}$: 7.8 Hz, $J_{5,4}$: 5.8 Hz, 1H, H-5), 4.35 (dd, J_{gem} : 12.1 Hz, $J_{8a,4}$: 3.3 Hz, 1H, H-8a), 4.48 (dd, J_{gem} : 12.1 Hz, $J_{8b,4}$: 7.9 Hz, 1H, H-8b), 4.60 (ddd, $J_{4,8b}$: 7.9 Hz, $J_{4,5}$: 5.8 Hz, $J_{4,8a}$: 3.3 Hz, 1H, H-4); ms, m/e 283 (M^+ +1, 15.4), 182 (1.6), 181 (6.7), 167 (5.9), 152 (5.9), 137 (4.2), 97 (4.6), 85 (10.7), 84 (30.8), 83 (100), 69 (23.4), 67 (11.0), 57 (69.4), 55 (23.7), 43 (13.8), 41 (56.2).

The second fraction gave (-)-**9a** (108 mg, 36% yield) as a colorless needles; m.p. 89-91°C; $(\alpha)_D$ -42.75 (c 1.2 in chloroform); ir (KBr): 2951, 2929, 2873, 1765, 1724, 1481, 1458, 1373, 1332, 1283, 1231, 1173, 1151, 1057, 1003, 950 cm^{-1} ; pmr (80 MHz) 1.0 (s, 3H), 1.05 (s, 6H), 1.2 (s, 9H, $(\text{CH}_3)_3\text{C}$), 1.21 (s, 3H), 2.4 (dd, $J_{5,1}$: 8.5 Hz, $J_{5,4}$: 2.0 Hz, 1H, H-5), 2.7 (d, $J_{1,5}$: 8.5 Hz, 1H, H-1), 3.9 (dd, J_{gem} : 12.2 Hz, $J_{8a,4}$: 3.6 Hz, 1H, H-8a), 4.1 (dd, J_{gem} : 12.2 Hz, $J_{8b,4}$: 3.7 Hz, 1H, H-8b), 4.6 (ddd, $J_{4,8a}$: 3.7 Hz, $J_{4,8b}$: 3.7 Hz, $J_{4,5}$: 2.0 Hz, 1H, H-4); cmr (20 MHz) 20.4, 20.7, 26.0, 26.9, 27.1, 38.8, 40.0, 41.3, 43.7, 46.8, 66.0, 77.2, 177.3, 178.0; ms, m/e 283 (M^+ +1, 1.2), 182 (0.5), 181(2.3), 167 (3.6), 152 (3.5), 137 (1.5), 85 (9.4), 84 (27.7), 83 (100), 69 (23.8), 57 (76), 55 (23.6), 43 (12.7), 41 (62.6). Anal. Calc. $\text{C}_{16}\text{H}_{26}\text{O}_4$: C, 68.08; H, 9.21. Found: C, 68.18; H, 9.49.

(1*S*,4*S*,5*R*)-4-trifluoroacetyloxymethyl-6,6,7,7-tetramethyl-3-oxabicyclo[3.2.0]heptan-2-one, 10a and (1*R*,4*S*,5*S*)-4-trifluoroacetyloxymethyl-6,6,7,7-tetramethyl-3-oxabicyclo[3.2.0]heptan-2-one, 10b.

A solution of freshly distilled **5** (315 mg, 1.5 mmol) and TME (1.9 mL, 16.02 mmol) in dry ether (45 mL) was irradiated at -20 °C for 2 h through quartz. After concentration, the crude was chromatographed on silica gel (0→15% ethyl acetate in hexane as eluent). The first fraction gave **10b** (13 mg, 3% yield); ir (film) 2983, 2964, 1793, 1771, 1300, 1208, 1139 cm^{-1} ; pmr (400 MHz) 1.02 (s, 3H), 1.05 (s, 3H), 1.1 (s, 3H), 1.20 (s, 3H), 2.75 (d, $J_{1,5}$: 7.9 Hz, 1H, H-1), 2.89 (dd, $J_{5,1}$: 7.9 Hz, $J_{5,4}$: 6.0 Hz, 1H, H-5), 4.50 (dd, J_{gem} : 12.0 Hz, $J_{8a,4}$: 3.1 Hz, 1H, H-8a), 4.70 (ddd, $J_{4,8b}$: 8.4 Hz, $J_{4,5}$: 6.0 Hz, $J_{4,8a}$: 3.1 Hz, 1H, H-4), 4.86 (dd, J_{gem} : 12.0 Hz, $J_{8b,4}$: 8.4 Hz, 1H, H-8b); ms, m/e 181 (M^+ -113, 2), 152 (2), 121

(2), 97 (4), 95 (2), 84 (27), 83 (100), 81 (11), 69 (35), 55 (14). The second fraction gave **10a** (75 mg, 17% yield); ir (film) 2963, 1794, 1770, 1348, 1225, 1166 cm^{-1} ; pmr (80 MHz) 1.0 (s, 3H), 1.1 (s, 6H), 1.2 (s, 3H), 2.5 (dd, $J_{5,1}$: 7.6 Hz, $J_{5,4}$: 1.7 Hz, 1H, H-5), 2.8 (d, $J_{1,5}$: 7.6 Hz, 1H H-1), 4.3 (dd, J_{gem} : 12 Hz, $J_{8a,4}$: 4.3 Hz, 1H, H-8a), 4.5 (dd, J_{gem} : 12.0 Hz, $J_{8b,4}$: 3.8 Hz, 1H, H-8b), 4.8 (ddd, $J_{4,8a}$: 4.3 Hz, $J_{4,8b}$: 3.8 Hz, $J_{4,5}$: 1.7 Hz, 1H, H-4); ms, m/e 181 (M^+ -113, 2), 152 (2), 125 (1), 100 (2), 97 (4), 84 (19), 83 (100), 81 (20), 79 (9), 69 (28), 55 (14).

These cycloadducts are extremely sensitive to hydrolysis, yielding of **7a** and **7b** that were isolated and detected by spectroscopic data.

(1R,4R,5S)-4-methyl-3-oxabicyclo[3.2.0]heptan-2-one, **11a** and (1S,4R,5R)-4-methyl-3-oxabicyclo[3.2.0]heptan-2-one, **11b**.

A solution of **1** (195 mg, 1.98 mmol) in dry ether (45 mL) was irradiated through quartz at $-78\text{ }^\circ\text{C}$ for 1 h with introduction of ethylene. Glc analysis of the crude indicated the presence of many by-products. The solvent was removed under reduced pressure to afford a residue, which was chromatographed on silica gel (mixtures of hexane-ether as eluents). The first fraction gave **11a** (75 mg, 30% yield) as a liquid which was contaminated by some by-products; ir (film) 2975, 2930, 1775, 1376, 1154 cm^{-1} ; pmr (80 MHz) 1.25 (d, $J_{8,4}$: 6.3 Hz, 3H, H-8), 1.90-2.65 (m, 4H), 2.95-3.5 (m, 2H), 4.50 (dq, $J_{4,8}$: 6.3 Hz, $J_{4,5}$: 1.0 Hz, 1H, H-4). The second fraction gave **11b** (45 mg, 18% yield) contaminated also by some by-products; ir (film) 2974, 2877, 1775, 1170, 1130 cm^{-1} ; pmr (80 MHz) 1.32 (d, $J_{8,4}$: 6.1 Hz, 3H), 1.70-2.70 (m, 4H), 2.85-3.40 (m, 2H), 4.60 (dq, $J_{4,8}$: 6.1 Hz, $J_{4,5}$: 5.7 Hz, 1H, H-4). All attempts to purify these cycloadducts from the by-products were unsuccessful.

(-)-(1R,4S,5S)-4-acetyloxymethyl-3-oxabicyclo[3.2.0]heptan-2-one, **12a** and (1S,4S,5R)-4-acetyloxymethyl-3-oxabicyclo[3.2.0]heptan-2-one, **12b**.

A solution of **3** (188 mg, 1.20 mmol) in freshly distilled acetone (45 mL) was irradiated through pyrex at $-78\text{ }^\circ\text{C}$ for 2 h with introduction of ethylene. The solvent was removed at reduced pressure and the crude was chromatographed on silica gel (mixtures of ethyl acetate-hexane as eluents). From the rapidly eluted fractions, **12a** (77 mg, 35% yield) was obtained as a colorless oil; b.p. 115-125 $^\circ\text{C}/0.2\text{ torr}$; $\{\alpha\}_D -43.9$ (c 1.3 in chloroform); ir (film) 2951, 1769, 1743, 1384, 1370, 1231, 1073 cm^{-1} ; pmr (400 MHz) 2.05 (s, 3H), 2.10 (m, 2H), 2.95 (m, 1H), 3.1 (m, 1H), 4.05 (dd, J_{gem} : 12.1 Hz, $J_{8a,4}$: 4.3 Hz, 1H, H-8a), 4.16 (dd, J_{gem} : 12.1 Hz, $J_{8b,4}$: 3.2 Hz, 1H, H-8b), 4.55 (ddd, $J_{4,8a}$: 4.3 Hz, $J_{4,8b}$: 3.2 Hz, $J_{4,5}$: 1.0 Hz, 1H, H-4); cmr (20 MHz) 20.4, 23.5, 24.6, 36.5, 38.6, 75.4, 82.3, 170.1, 179.5; ms m/e 142 (M^+ +1-43, 3), 124 (11), 112 (7), 111 (100), 84 (5), 83 (51), 79 (5), 55 (41), 43 (67). Anal. Calc. for $\text{C}_9\text{H}_{12}\text{O}_4$: C, 58.69; H, 6.57. Found: C, 58.65; H, 6.60.

From the slowly eluted fractions, **12b** (25 mg, 11% yield) was obtained as an oil that was

unsuitable for optical rotation measurements; ir (film) 2924, 1770, 1742, 1370, 1233, 1074 cm^{-1} ; pmr (400 MHz) 2.07 (s, 3H), 2.08 (m, 2H), 2.15 (m, 1H), 2.5 (m, 1H), 3.15 (m, 1H), 3.25 (m, 1H), 4.21 (dd, J_{gem} : 12.2 Hz, $J_{8a,4}$: 4.3 Hz, 1H, H-8a), 4.30 (dd, J_{gem} : 12.2 Hz, $J_{8b,4}$: 7.8 Hz, 1H, H-8b), 4.6 (ddd, $J_{4,8b}$: 7.8 Hz, $J_{4,5}$: 5.6 Hz, $J_{4,8a}$: 4.3 Hz, 1H, H-4); cmr (20 MHz) 19.2, 23.0, 24.6, 36.3, 39.6, 62.9, 78.4, 170.2, 179.4; ms m/e 185 ($M^+ + 1$, 0.2), 143 (1), 142 (7), 124 (27), 112 (7), 111 (100), 96 (14), 84 (6), 83 (52), 79 (12), 55 (47), 43 (93).

(1R,4S,5S)-4-pivaloyloxymethyl-3-oxabicyclo[3.2.0]heptan-2-one, **13a** and (1S,4S,5R)-4-pivaloyloxymethyl-3-oxabicyclo[3.2.0]heptan-2-one, **13b**.

A solution of **4** (220 mg, 1.12 mmol) in freshly distilled acetone (45 mL) was irradiated through pyrex at $-78\text{ }^\circ\text{C}$ for 1.5 h with introduction of ethylene. The solvent was eliminated under reduced pressure to afford a crude, which was chromatographed on silica gel (mixtures of hexane-ether as eluents) to give (124 mg, 49% yield) of a mixture of the diastereomers; 100-120 $^\circ\text{C}/0.02$ torr. Anal. Calc. for $\text{C}_{12}\text{H}_{18}\text{O}_4$: C, 63.70; H, 8.01. Found: C, 63.79; H, 8.00. All attempts to separate these compounds were unsuccessful and enriched fractions were analyzed. **13a**: ir (film) 2975, 2874, 1775, 1732, 1470, 1459, 1399, 1364, 1336, 1280, 1148, 1071, 1030, 941, 770 cm^{-1} ; pmr (400 MHz) 1.3 (s, 9H, $(\text{CH}_3)_3\text{C}$), 2.15 (m, 2H), 2.42 (m, 1H), 2.56 (m, 1H), 2.96 (m, 1H), 3.15 (m, 1H), 4.05 (dd, J_{gem} : 12 Hz, $J_{8a,4}$: 3.2 Hz, 1H, H-8a), 4.2 (dd, J_{gem} : 12 Hz, $J_{8b,4}$: 3.2 Hz, 1H, H-8b), 4.59 (ddd, $J_{4,8a}$: 3.2 Hz, $J_{4,8b}$: 3.2 Hz, $J_{4,5}$: 1.2 Hz, 1H, H-4); cmr (20 MHz) 23.6, 24.8, 27.0, 36.5, 38.7, 38.9, 65.3, 82.6, 177.9, 179.5; ms, m/e 227 ($M^+ + 1$, 9.5), 182 (0.2), 125 (4.4), 124 (27.1), 111 (77.5), 96 (13.3), 85 (13.2), 83 (37.9), 79 (13.6), 69 (11.7), 57 (100), 55 (46.1), 43 (14.5), 41 (57.7). **13b**: ir (film) 2975, 2874, 1775, 1732, 1470, 1459, 1399, 1364, 1336, 1280, 1148, 1071, 1030, 941, 770 cm^{-1} ; pmr (400 MHz) 1.35 (s, 9H, $(\text{CH}_3)_3\text{C}$), 2.05-2.3 (m, 2H), 2.4-2.52 (m, 2H), 3.1-3.25 (m, 2H), 4.22 (dd, J_{gem} : 11.9 Hz, $J_{8a,4}$: 4.8 Hz, 1H, H-8a), 4.28 (dd, J_{gem} : 11.9 Hz, $J_{8b,4}$: 7.3 Hz, 1H, H-8b), 4.62 (ddd, $J_{4,8b}$: 7.3 Hz, $J_{4,5}$: 5.2 Hz, $J_{4,8a}$: 4.8 Hz, 1H, H-4); cmr (20 MHz) 19.2, 23.0, 27.0, 36.4, 38.7, 39.5, 62.7, 78.4, 177.8, 179.2; ms, m/e 227 ($M^+ + 1$, 9.5), 182 (0.2), 125 (4.4), 124 (27.1), 111 (77.5), 96 (13.3), 85 (13.2), 83 (37.9), 79 (13.6), 69 (11.7), 57 (100), 55 (46.1), 43 (14.5), 41 (57.7).

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