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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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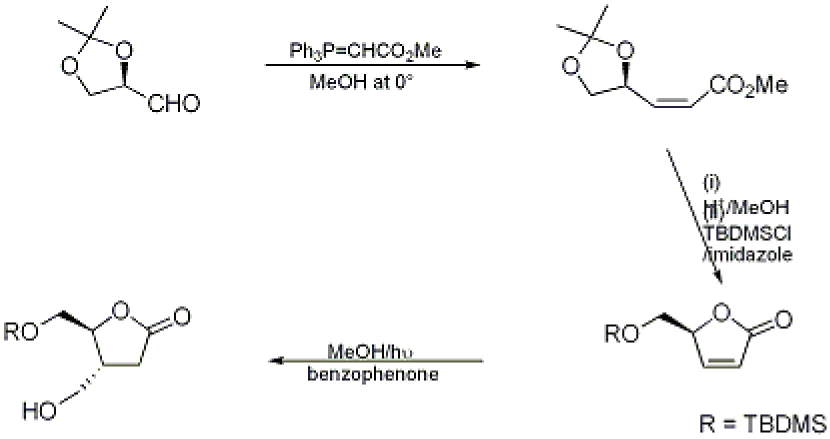
PHOTOINDUCED-ADDITION OF METHANOL TO (5S)-(5-O-tert-BUTYLDIMETHYLSILOXYMETHYL)FURAN-2(5H)-ONE: (4R,5S)-4-HYDROXYMETHYL-(5-O-tert-BUTYLDIMETHYLSILOXYMETHYL)FURAN-2(5H)-ONE

[2(5H)-Furanone, 5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-, (S)- and D-erythro-Pentonic acid, 2,3-dideoxy-5-O-[(1,1-dimethylethyl)dimethylsilyl]-3-(hydroxymethyl)-, γ-lactone]



Submitted by John Mann and Alexander C. Weymouth-Wilson[1] .
Checked by Robert E. Koehler, Steven Wolff, and David L. Coffen.

1. Procedure

(5S)-(5-O-tert-Butyldimethylsiloxymethyl)furan-2(5H)-one (Note 1). An oven-dried, 500-mL, round-bottomed flask is charged with 35.5 g (0.27 mol) of 2,3-O-isopropylidene-D-glyceraldehyde (Note 2) and 250 mL of methanol . The flask is cooled in an ice bath during the portionwise addition of 96 g (0.28 mol) of methyl (triphenylphosphoranylidene)acetate (Note 3), and the resultant mixture is stirred for 1 hr at 0°C. The solvent is removed on a rotary evaporator and the residue is refluxed for 30 min with a mixture of ether:petroleum ether (3:7, 100 mL). The process is repeated three times, the combined extracts are filtered, and the filtrate is concentrated to yield a colorless oil. The oil is purified by silica chromatography [1 kg of silica, 8.5-cm × 43-cm column eluting with ethyl acetate:petroleum ether (3:7)] to yield 39.5 g (78%) of methyl (4S)-4,5-O-isopropylidenepent-(2Z)-enoate , and 4.8 g (10%) of the corresponding trans-isomer, both as colorless oils (Note 4), (Note 5).

A solution of 39.0 g (0.21 mol) of the cis-alkene in 100 mL of methanol is treated with concd sulfuric acid (ca. 0.8 mL of 30%), and the mixture is stirred for 2 hr at room temperature. Evaporation of the solvent and purification of the residue by silica chromatography (1 kg of silica, 8.5-cm × 43-cm column with ethyl acetate as eluant) yield 22.3 g (93%) of (S)-5-hydroxymethylfuran-2(5H)-one as a white crystalline solid, mp 40-41°C and $[\alpha]_D^{20}$ −150.8° (water, *c* 2.1) (Note 6).

A solution of 22.0 g of the alcohol (0.19 mol) and 17.6 g (0.26 mol) of imidazole in dichloromethane (Note 7) (100 mL) is cooled in an ice bath, and 36.2 g (0.24 mol) of tert-butyldimethylsilyl chloride (Note 8) is added in one portion. The mixture is stirred for 15 min at 0°C and for a further 20 min at room temperature. Water (200 mL) is then added, and the organic layer is separated. The aqueous layer is extracted with dichloromethane (3 × 50 mL), and the combined organic extracts are dried over sodium sulfate prior to evaporation of the solvent. Purification of the residue by silica chromatography [1 kg of silica, 8.5-cm × 43-cm column eluting with ethyl acetate:petroleum ether (3:7)] yields 45 g (ca. ~ 100%) of (5S)-(5-O-tert-butyldimethylsiloxymethyl)furan-2(5H)-one as a colorless solid, mp 31°C and $[\alpha]_D^{20}$ −146° (in chloroform , *c* 0.2) (Note 9).

(4R,5S)-4-Hydroxymethyl-(5-O-tert-butyldimethylsiloxymethyl)furan-2(5H)-one . A 1-L Pyrex vessel is charged with 29.5 g (0.13 mol) of (5S)-(5-O-tert-butyldimethylsiloxymethyl)furan-2(5H)-one , 23.7 g (0.13 mol) of benzophenone (Note 10) and 800 mL of methanol . The vessel is placed in a water-cooled, immersion-irradiation apparatus (Note 11), and the solution is degassed for 1 hr in a stream of nitrogen. It is then irradiated using two 125-watt, 350-nm lamps; the reaction is complete after 48 hr (Note 12). The solvent is evaporated and the residue is purified by silica chromatography [1 kg of silica, 8.5-cm × 43-cm column with a gradient elution from ethyl acetate:petroleum ether (1:1) to neat ethyl acetate]. This yields 18.5 g (55%) of the title compound, 18.3 g (77%) of recovered benzophenone, 3.6 g of benzpinacol , and 1.56 g (3%) of the photoadduct (4R,5S)-4-diphenylhydroxymethyl-5-tert-butyldimethylsiloxymethylfuran-2(5H)-one . The title photoadduct is an oil with $[\alpha]_D^{20}$ +3.2° (in chloroform, *c* 2.0) (Note 13).

2. Notes

1. (5S)-(5-O-tert-Butyldimethylsiloxymethyl)furan-2(5H)-one has been prepared by a number of groups.[2] They report mp of 31-32°C and 31°C, and $[\alpha]_D^{20}$ of −141° and −139°.
2. 2,3-O-Isopropylidene-D-glyceraldehyde was prepared as described in *Org. Synth.* **1995**, *72*, 6.
3. This compound was purchased from Aldrich Chemical Company, Inc.
4. The submitters report that they currently use two 500-g columns run consecutively. After the first column is used, it is washed with methanol, all traces of solvent flushed through with compressed air, reequilibrated with eluant, then those fractions (from the first column) that contain a mixture of cis- and trans-alkenes are rechromatographed.
5. The cis-alkene has the following spectral features: IR (thin film) cm^{-1}: 1725, 1650, 1210, 1065 ; ^{1}H NMR (220 MHz, $CDCl_3$) δ: 1.40 and 1.46 (2 s, 6 H, 2 × Me), 3.65 (dd, 1 H, J_{gem} 8.5, $J_{4,5}$ 7, 5-H), 3.75 (s, 3 H, OMe), 4.40 (dd, 1 H, $J_{4,5}$ 7, 5-H), 5.52 (m, 1 H, 4-H), 5.88 (dd, 1 H, $J_{2,3}$ 11.5, $J_{2,4}$ 1.5, 2-H), 6.39 (dd, 1 H, $J_{2,3}$ 11.5, $J_{3,4}$ 6.5, 3-H) .
6. (S)-5-Hydroxymethylfuran-2(5H)-one has the following spectral data: IR (KBr disc) cm^{-1}: 3420, 1790, 1605, 1170, 1115, 1080, 1060, 865 ; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.70-4.06 (m, 3 H, 5-H and OH), 5.19 (m, 1 H, 4-H), 6.20 (dd, 1 H, $J_{2,3}$ 5.5, $J_{2,4}$ 2, 2-H), 7.56 (dd, 1 H, $J_{2,3}$ 5.5, $J_{3,4}$ 1.5, 3-H) . This compound is available from Aldrich Chemical Company, Inc., and has been prepared by a number of other groups.[3] They report mp ranging from 39° to 42°C, and $[\alpha]_D^{20}$ values from −140° to −154.5°.
7. Dichloromethane was dried over phosphorus pentoxide .
8. tert-Butyldimethylsilyl chloride was purchased from Aldrich Chemical Company, Inc.
9. Spectral data for the silyl ether are as follows: IR (nujol mull) cm^{-1}: 1747, 1605, 1473, 1331, 1135, 1016, 888 ; ^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.02 (s, 3 H, Me), 0.03 (s, 3 H, Me), 0.83 (s, 9 H, tert-Bu), 3.76 (dd, 1 H, J_{gem} 10.8, $J_{4,5}$ 5, 5-H), 3.86 (dd, 1 H, $J_{4,5}$ 5-H), 5.04 (m, 1 H, 4-H), 6.11 (dd, 1 H, $J_{2,3}$ 5.7 $J_{2,4}$ 1.95, 2-H), 7.49 (dd, 1 H, $J_{2,3}$ 5.7, $J_{3,4}$ 1.4, 3-H) .
10. Use of less than one equivalent of benzophenone increases the photolysis time.
11. The checkers employed a Hanovia 450W medium-pressure mercury arc lamp with an uranium glass filter, a Pyrex immersion well, and a 1-L irradiation vessel (all available from Ace Glass).
12. Use of larger wattage lamps decreases the photolysis time.
13. Spectral data for the photoadduct are as follows: IR cm^{-1}: 3430, 1760, 1470, 1410, 1380, 1258, 1121, 1020, 940, 875, 838, 778 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.04 (s, 3 H, Me), 0.05 (s, 3 H, Me), 0.86 (s, 9 H, tert-Bu), 2.29 (dd, 1 H, J_{gem} 17, $J_{3,4}$ 4.6, 3-H), 2.63 (m, 2 H, 4-H and OH), 2.69 (dd, 1 H, $J_{3,4}$ 9.4, 3-H), 3.60 (dd, 1 H, J_{gem} 10.5, $J_{4,7}$ 6.6, 7-H), 3.66 (dd, 1 H, $J_{4,7}$ 5.2, 7-H), 3.72 (dd, 1 H, J_{gem} 11.2, $J_{5,6}$ 2.9, 6-H), 3.83 (dd, 1 H, $J_{5,6}$ 3.7, 6-H), 4.39 (dt, 1 H, $J_{5,6}$ 3.7, $J_{4,5}$ 3.2, 5-H) .

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

The photoinduced-addition of alcohols to cycloalkenones has been investigated by Fraser-Reid and co-workers,[4] by Paquette,[5] and was used as the key step in the synthesis of the prostaglandin endoperoxide analogue (15S)-hydroxy-9α,11α-epoxymethanoprosta-(5Z,13E)-dienoic acid,[6] and for the recent synthesis of 2',3'-dideoxy-3'-hydroxymethyl-5'-carbanucleosides.[7] No work (other than our own) has been reported on the photoinduced-addition of alcohols to 5-substituted furan-2(5H)-ones.

The reaction appears to be general and the additions are regiospecific and stereoselective. The product from the reaction with 2-propanol has been used for the synthesis of cis-chrysanthemic acid ,[8] and the product with methanol has been used for the construction of novel 2',3'-dideoxy-3'-hydroxymethylnucleosides .[9] In addition, ethane-1,2-diol provides the expected photoadduct as a 1:1 mixture of the two possible diastereoisomers, and these can be easily separated as their acetonides, to provide compounds with three contiguous chiral centers emanating from furan-ones with only one chiral center.[9] More recently, we have shown that photoinduced-additions also occur with cyclic amines[10] and these reactions provide access to the skeletons of the pyrrolizidine and indolizidine alkaloids in a concise and stereochemically efficient fashion.

These photoinduced reactions proceed in fair to good yields (50-80%) and tolerate a variety of protecting groups at C-6, e.g., acetate, benzoate, methyl, and benzyl.

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

(5S)-(5-O-tert-Butyldimethylsiloxymethyl)furan-2(5H)-one:
2(5H)-Furanone, 5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-, (S)- (11); (105122-15-4)

(4R,5S)-4-Hydroxymethyl-(5-O-tert-butyldimethylsiloxymethyl)furan-2(5H)-one:
D-erythro-Pentonic acid, 2,3-dideoxy-5-O-[(1,1-dimethylethyl)dimethylsilyl]-3-hydroxymethyl)-, γ-lactone (13); (164848-06-0)

L-(S)-Glyceraldehyde acetonide:

1,3-Dioxolane-4-carboxaldehyde, 2,2-dimethyl-, L- (8);
1,3-Dioxolane-4-carboxaldehyde, (S)- (9); (22323-80-4)

Methyl (triphenylphosphoranylidene)acetate:
Acetic acid, (triphenylphosphoranylidene), methyl ester (8);
Propanoic acid, 2-(triphenylphosphoranylidene)-, methyl ester (9); (2605-67-6)

Methyl (4S)-4,5-O-isopropylidenepent-(2Z)-enoate:
2-Propenoic acid, 3-(2,2-dimethyl-1,3-dioxolan-4-yl)-, methyl ester, [S-(Z)]- (11); (81703-94-8)

(S)-5-Hydroxymethylfuran-2(5H)-one:
2(5H)-Furanone, 5-(hydroxymethyl)-, (S)- (10); (78508-96-0)

tert-Butyldimethylsilyl chloride:
Silane, chloro(1,1-dimethylethyl)dimethyl- (9); (18162-48-6)

Benzophenone (8);
Methanone, diphenyl- (9); (119-61-9)