

18. A Stereoselective Approach to the Spiro [4,5]decane System via Intramolecular Photocycloaddition and Reductive Fragmentation

Preliminary communication

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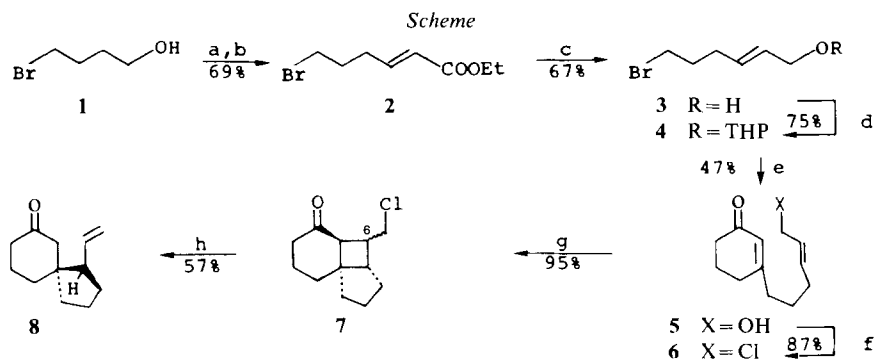
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Summary

The photoaddition $6 \rightarrow 7$, followed by a reductive cleavage of the γ -chlorocyclobutylketone **7**, gave the stereochemically pure spiro [4,5]decane **8**.

Intramolecular (2+2)-photoadditions combined with a selective cyclobutane cleavage have been applied only recently to the synthesis of complex ring systems such as the natural products (+)-longifolene [1], (+)-sativene [1b], (\pm)- β -bulnesene [2] and (\pm)-isocomene [3]¹. We further envisaged the exploitation of regio- and stereoselective intramolecular enone-ene-photocycloadditions to prepare γ -halocyclobutyl ketones which should be suitable for a new reductive fragmentation². The feasibility of this approach is demonstrated here by the successful synthesis of the bifunctional spiro compound **8**.

Oxidation of 4-bromobutanol (**1**) [6] with pyridinium chlorochromate [7] (1.05 mol-equiv.) followed by a *Horner-Emmons* reaction of the resulting crude aldehyde using triethylphosphonoacetate (1.0 mol-equiv.) and NaH (1.0 mol-equiv.)



a) PCC, CH₂Cl₂, 25°, 90 min. b) (EtO)₂P-CH₂-COOEt, NaH, THF, -20°, 2 h. c) DIBAH, hexane, 0°, 1 h. d) DHP, TsOH, CH₂Cl₂, 25°, 20 h. e) Mg, THF; 3-ethoxy-2-cyclohexenone, 2 h, 25°; 10% aq. HCl, 25°, 15 min; MeOH, TsOH, 25°, 1 h. f) NCS, CH₂Cl₂, Me₂S. g) hv, Hg medium-pressure lamp, C₆H₆. h) Li, NH₃, THF, -78°, 30 min.

¹) For further combinations of intramolecular photocycloadditions and cleavage reactions, see [4].

²) For the reductive cleavage of cyclobutanes bearing carbonyl groups in a 1,4-relationship, see [4b,j] and [5].

in THF gave the pure (*E*)-ester **2**³) in 69% overall yield. Reduction of ester **2** with diisobutylaluminium hydride (2.2 mol-equiv.) in hexane at 0° furnished the allylic alcohol **3**³) (67%) which, on acid-catalyzed acetalization with dihydropyran (1.1 mol-equiv.), afforded the bromotetrahydropyranyl ether **4**³) in 75% yield (40% overall yield from **1**). The 3-(4'-alkenyl)-2-cyclohexen-1-one **5**³) was prepared by successive addition of the *Grignard* reagent derived from **4** (1.2 mol-equiv. in THF) to 3-ethoxy-2-cyclohexenone, treatment with aq. 10% HCl-solution, and acetal cleavage by methanolysis (0.4% *p*-toluenesulfonic acid in methanol, 25°). Conversion of the alcohol **5** to the allylic chloride **6**³) was accomplished in 87% yield with retention of both regio and stereochemical integrity using the complex formed from *N*-chlorosuccinimide and dimethyl sulfide [8] (3.8 mol-equiv., CH₂Cl₂, 0°, 45 min). The crucial (2+2)-cycloaddition of dienone **6** proceeded smoothly and efficiently on irradiation in benzene through a *Pyrex* filter using a medium-pressure mercury lamp (*Philips* 125 W, 1.5 h) to give the tricyclo[5.4.0.0^{1,5}]undecanone **7**³) in 95% yield as an 4:1 isomer mixture. Both isomers, separated by chromatography (SiO₂, toluene/ethyl acetate 19:1) showed an IR. absorption for an unstrained C=O group at 1705 cm⁻¹. This, together with analogous photoadditions [4e] [9] led us to assume that the cyclobutane is *cis*-fused to the 5- as well as to the 6-membered ring in both photoproducts **7** which thus appear to be C(6)-epimers. Reductive cleavage of the mixture **7** using excess lithium in dry NH₃/THF 2:1 (-78°, 1 h) followed by quenching with solid NH₄Cl and work-up, gave the spiroketone **8**³)⁴) as a single isolable product (57%).

Further studies on the stereochemical details and synthetic applicability of this photoaddition-cleavage sequence are under way.

Financial support of this work by the *Swiss National Science Foundation*, *Sandoz Ltd*, Basel and *Givaudan SA*, Vernier, is gratefully acknowledged.

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³) IR., ¹H-NMR. and MS. are in full agreement with the assigned structure.

⁴) IR. (CCl₄, $\tilde{\nu}_{\max}$ in cm⁻¹): 1715s, 918m. - NMR. spectra in CDCl₃, internal standard tetramethylsilane ($\delta=0$ ppm); abbreviations: s=singlet, d=doublet, t=triplet, m=multiplet, J=spin-spin coupling constant (Hz): ¹H-NMR. (100 MHz): 1.1-2.5 (15 H); 5.1 (m, 2 H); 5.7 (m, 1 H). - ¹³C-NMR. (25.2 MHz): 211.7 (s), 138.4 (d), 116.2 (t), 54.5 (d), 50.1 (s), 47.1 (t), 41.2 (t), 35.9 (t), 29.7 (t), 23.5 (t), 21.5 (t).