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

Preliminary communication

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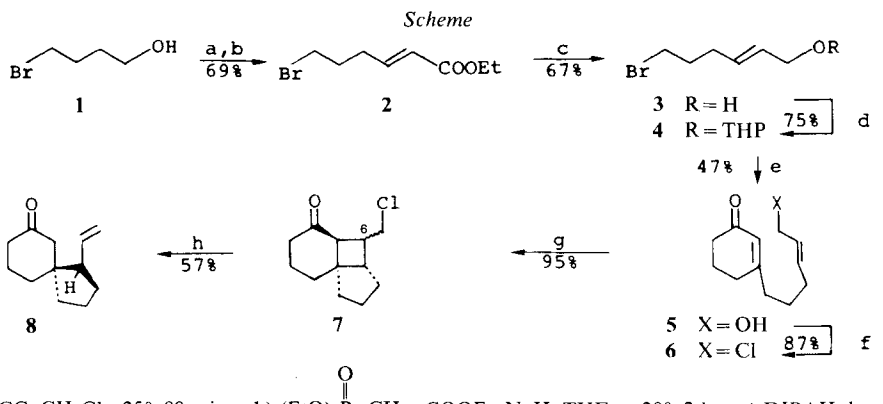
Summary

The photoaddition **6**→**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], (±)-β-bulnesene [2] and (±)-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 fragmentation[2]). 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.)

Scheme



a) PCC, CH_2Cl_2, 25°, 90 min. b) $(EtO)_2\overset{O}{\overset{\|}{P}}-CH_2-COOEt$, NaH, THF, −20°, 2 h. c) DIBAH, hexane, 0°, 1 h. d) DHP, TsOH, CH_2Cl_2, 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, CH_2Cl_2, Me_2S. g) hν, Hg medium-pressure lamp, C_6H_6. h) Li, NH_3, 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].

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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., CH_2Cl_2, 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 (SiO_2, 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 NH_3/THF 2:1 (−78°, 1 h) followed by quenching with solid NH_4Cl 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.

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[3]) IR., ^{1}H-NMR. and MS. are in full agreement with the assigned structure.

[4]) IR. (CCl_4, $\tilde{\nu}_{max}$ in cm^{-1}): 1715*s*, 918*m*. – NMR. spectra in $CDCl_3$, internal standard tetramethylsilane ($\delta = 0$ ppm); abbreviations: *s* = singlet, *d* = doublet, *t* = triplet, *m* = multiplet, *J* = spin-spin coupling constant (Hz): ^{1}H-NMR. (100 MHz): 1.1–2.5 (15 H); 5.1 (*m*, 2 H); 5.7 (*m*, 1 H). – ^{13}C-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*).