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SHORT COMMUNICATIONS

Synthesis of (+)-(1*S*,4*R*)-1-(1-Chlorovinyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-one

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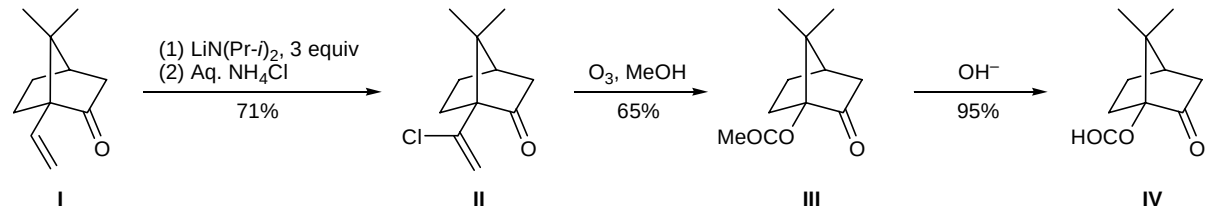
7,7-Dimethyl-1-vinylbicyclo[2.2.1]heptan-2-one (**I**) which is readily accessible from *d*-camphorsulfonic acid [1] is extensively used in the synthesis of taxoids [2, 3] and their precursors [4]. No specific chemical properties of keto olefin **I** have been noted; for example, by the action of deprotonating agents it gives rise to expected enolates which are involved in reactions typical of such derivatives [5, 6]. While trying to effect Michael reaction of methyl propynoate with the enolate generated from ketone **I** by the action of lithium diisopropylamide (LDA), we have found that the process takes an unexpected path. After treatment of the reaction mixture with an aqueous solution of NH_4Cl and purification of the crude product on silica gel, we isolated (+)-(1*S*,4*R*)-1-(1-chlorovinyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-one (**II**) in a moderate yield. Clearly, methyl propynoate does not participate in this transformation. Therefore, we carried out the reaction under analogous conditions but without addition of methyl propynoate. Compound **I** was treated with 3 equiv of LDA in THF at –78 to 20°C over a period of 1 h; the mixture was then kept for 12 h at 20°C and was treated with an aqueous solution of ammonium chloride. As a result, we isolated chlorine-containing ketone **II** in a good yield. When water was used instead of aqueous NH_4Cl for quenching of the reaction mixture, initial ketone **I** was recovered from the mixture. The yield of **II** did not change on replacement of LDA by Et_2NLi; no reaction occurred with $NaN(Pr\text{-}i)_2$. Compound **II** was not formed when ketone **I** was added to the system solid NH_4Cl–LDA or solid NH_4Cl–solid LiOH–*i*-Pr_2NH in THF, which was prepared preliminarily under argon. The structure of ketone **II** was confirmed by the spectral data and chemical reactions, specifically by the transformation of **II** into ester **III** and acid **IV** [8, 9]. Chlorovinyl ketone **II** attracts interest primarily as a new chiral initial compound in target-oriented syntheses. Presumably, the mechanism of formation of compound **II** involves generation of hypochlorite-like chlorinating intermediates during treatment of the reaction mixture with aqueous ammonium chloride.

(+)-(1*S*,4*R*)-1-(1-Chlorovinyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-one (II). To a solution of 191 mg (1.89 mmol) of diisopropylamine in 5 ml of tetrahydrofuran we added at 0°C under argon 0.59 ml (1.83 mmol) of a 3.1 N solution of butyllithium in hexane. The mixture was stirred for 15 min and cooled to –78°C, and a solution of 100 mg (0.61 mmol) of olefin **I** in 5 ml of THF was added dropwise to the resulting solution of lithium diisopropylamide. The mixture was stirred for 30 min, allowed to warm up to 20°C, kept for 12 h at that temperature, and treated with 5 ml of a saturated aqueous solution of ammonium chloride. The solvent was distilled off, and the aqueous phase was extracted with ethyl acetate (3× 10 ml). The extract was dried over $MgSO_4$, the solvent



I **II** **III** **IV**

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was distilled off, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (10:1) as eluent. Yield 86 mg (71%), mp 59–60.5°C (from hexane), R_f 0.61 (hexane–EtOAc, 5:1), $[\alpha]_D^{20}$ = +100° (*c* = 1, $CHCl_3$). IR spectrum, ν, cm^{-1}: 1644, 1748. ^1H NMR spectrum, δ, ppm: 1.05 s (3H, CH_3), 1.07 s (3H, CH_3), 1.40 d.d.d (1H, *endo*-5-H, *J* = 3.9, 9.1, 12.6 Hz), 1.60 d.d.d (1H, *endo*-6-H, *J* = 4.5, 9.1, 13.5 Hz), 1.93 d (1H, *endo*-3-H, ^3J = 0.9, ^2J = 18.4 Hz), 2.10–2.30 m (2H, *exo*-5-H, *exo*-6-H), 2.40 m (1H, 4-H), 2.50 d.t (1H, *exo*-3-H, ^3J = 4.13, 18.4 Hz), 5.34 d (1H, ^2J = 1.5 Hz), 5.56 d (1H, $=CH_2$, ^2J = 1.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.05 q (CH_3), 21.63 q (CH_3), 26.54 t (C^5), 28.40 t (C^6), 43.75 t (C^3), 43.84 d (C^4), 49.55 s (C^7), 67.58 s (C^1), 117.54 t and 137.43 s ($C=CH_2$), 212.69 s (C^2). Mass spectrum (EI), *m*/*z* (I_{rel}, %): 198 (28) $[M]^+$, 183 (28) $[M - CH_3]^+$, 170 (12) $[M - C_2H_4]^+$, 163 (60) $[M - Cl]^+$, 155 (38), 41 (100). Found, %: C 66.29; H 7.55; Cl 17.49. $C_{11}H_{15}ClO$. Calculated, %: C 66.49; H 7.61; Cl 17.84.

Methyl 7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-carboxylate (III) and 7,7-dimethyl-2-oxobicyclo-[2.2.1]heptane-1-carboxylic acid (IV). A solution of 100 mg (0.51 mmol) of compound **II** in 5 ml of methanol was cooled to–78°C, and an ozone–oxygen mixture was passed through the solution until it became light blue. Excess ozone was removed by flushing with argon, and the mixture was allowed to gradually warm up to 20°C and was stirred for 2 days at that temperature. The solvent was distilled off, and the residue was subjected to chromatography on SiO_2 using petroleum ether–ethyl acetate (10:1) as eluent. Yield 77 mg (78%), mp 49–51°C (from hexane), R_f 0.72 (hexane–EtOAc, 5:1), $[\alpha]_D^{20}$ = +25.8° (*c* = 1, $CHCl_3$). ^1H NMR spectrum, δ, ppm: 1.05 s (3H, CH_3), 1.13 s (3H, CH_3), 1.40 d.d.d (1H, *endo*-6-H, *J* = 4.0, 9.5, 13.0 Hz), 1.75 d.d.d (1H, *endo*-7-H, *J* = 4.8, 9.5, 14.3 Hz), 1.93 d (1H, *endo*-4-H, ^3J = 0.9, ^2J = 18.4 Hz), 2.00–2.30 m (2H, *exo*-6-H, *exo*-7-H), 2.35 m (1H, 5-H), 2.50 d.t (1H, *exo*-4-H, *J* = 4.0, 18.4 Hz), 3.73 s (3H, OCH_3). ^{13}C NMR spectrum, δ_C, ppm: 19.66 (CH_3), 21.16 (CH_3), 26.30 (C^5, C^6), 43.78 (C^3), 44.18 (C^4), 49.12 (C^7), 51.76 (OCH_3), 67.03 (C^1), 170.15 (COO), 210.99 (C^2).

Acid **IV** was synthesized by alkaline hydrolysis of ester **III** under standard conditions. mp 225–228°C (from water); published data: mp 227–229°C [8].

The IR spectra were recorded on a UR-20 spectrophotometer from samples dispersed in mineral oil. The ^1H and ^{13}C NMR spectra were obtained on a Bruker AM-300 spectrometer (300 and 75.47 MHz for ^1H and ^{13}C, respectively) from solutions in $CDCl_3$ using TMS as internal reference. Silica gel L 100/160 μm (Lachema) was used for column chromatography. Thin-layer chromatography was performed on Silufol plates. The optical rotations were measured on a Perkin–Elmer 241 MC polarimeter. The mass spectrum (electron impact, 70 eV) was recorded on an MKh-1320 instrument.

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