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SHORT COMMUNICATIONS

New "Camphor" Michael Acceptor

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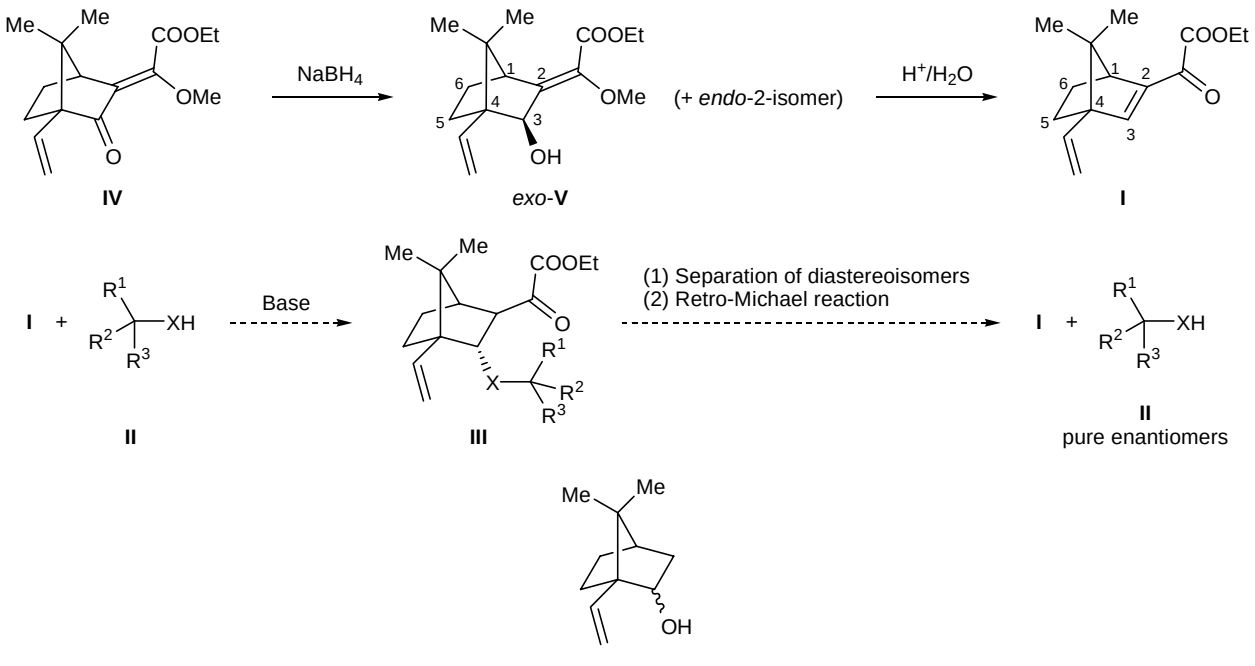
Camphor derivatives are widely used in organic synthesis as chiral auxiliaries for the preparation of optically active compounds from achiral substrates [1–5]. In such transformations, one of the two racemic reactants is usually linked to camphor derivative through a covalent bond. When the reaction is complete, the resulting diastereoisomers are separated, and the camphor residue is removed to isolate pure enantiomers. It should be noted that the camphor framework possesses excellent stereodifferentiating properties; therefore, most reactions at a prochiral center are highly diastereoselective, and there is no need of separating the diastereoisomeric pairs. In the present communication we describe a new camphor derivative **I** as a Michael acceptor which can be used for optical resolution of racemic alcohols, thiols, and amines **II**. After separation of diastereoisomers **III**, pure enantiomers of **II** can be isolated by treatment with a base. The main advantages of enone **I** as chiral auxiliary, which originate from its structure and functionalization pattern, are the expected high reactivity (it contains a powerful electron-acceptor group and an activated bornene-like double bond) and good stereocontrol in the transition state of the addition process due to effect of the camphor skeleton and side-chain substituents on the attack by nucleophile.

Compound **I** was synthesized by reduction of oxo ester **IV** [6] with sodium tetrahydridoborate, followed by acid hydrolysis of enol **V**. The reduction of **IV** yields preferentially the *exo* isomer of **V** (the ratio



X = NH, O, S.

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exo/*endo* is equal to 7:1). Stereochemical assignments in epimeric alcohols **VI**, which are structurally related to **V**, were discussed in [7].

Ethyl (1*S*,4*R*)-2-(7,7-dimethyl-4-vinylbicyclo-[2.2.1]hept-2-en-2-yl)-2-oxoacetate (I). Concentrated sulfuric acid, 0.1 ml, was added to a solution of 100 mg (0.36 mmol) of alcohol **V** in 6 ml of a 1:1 water–THF mixture. The mixture was heated for 1 h under reflux, the aqueous layer was neutralized to pH 6–7 with a saturated solution of $NaHCO_3$, the product was extracted into ethyl acetate (3×10 ml), the extract was dried over magnesium sulfate and evaporated under reduced pressure, and the residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (10:1) as eluent. Yield 79 mg (87%), R_f 0.61 (hexane–ethyl acetate, 5:1). $[\alpha]_D^{20}$ = –92° (*c* = 1.0, $CHCl_3$). IR spectrum, ν, cm^{-1}: 1666, 1732. ^1H NMR spectrum, δ, ppm: 0.80 s (CH_3), 0.87 s (CH_3), 1.05 m (1H), 1.25 m (1H), 1.45 t (3H, CH_3, *J* = 7 Hz), 2.00 m (2H), 3.00 d (1H, 1-H, *J* = 2.5 Hz), 4.35 q (2H, OCH_2, *J* = 2.5 Hz); 5.25 d.d (1H, *J* = 17.1, 1.3 Hz), 5.29 d.d (1H, *J* = 10.2, 1.3 Hz), 5.90 d.d (1H, *J* = 10.2, 17 Hz) ($CH=CH_2$); 7.28 d (1H, 2-H, *J* = 2.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.01 (CH_3), 19.31 (CH_3), 19.42 (CH_3), 24.30 (C^6), 29.77 (C^5), 51.07 (C^1), 58.43 (C^7), 61.93 (OCH_2), 63.03 (C^4), 116.87 and 134.85 ($CH_2=CH$), 144.96 (C^2), 155.87 (C^3), 162.50 and 181.76 ($COCO_2$). Found, %: C 72.65; H 8.11. $C_{15}H_{20}O_3$. Calculated, %: C 72.55; H 8.12.

Ethyl (1*S*,2*S*,4*S*)-2-(3-hydroxy-7,7-dimethyl-4-vinylbicyclo[2.2.1]hept-2-ylidene)-2-methoxyacetate (V). To a solution of 100 mg (0.36 mmol) of ketone **IV** in 4 ml of ethanol we added under stirring at 0°C 32 mg (0.85 mmol) of 85% $NaBH_4$. The mixture was allowed to warm up to room temperature and was stirred for 12 h. Excess $NaBH_4$ was decomposed with a saturated solution of ammonium chloride, ethanol was distilled off, and the product was extracted into ethyl acetate (3×10 ml). The extract was dried over magnesium sulfate and evaporated under reduced pressure, and the residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (10:1) as eluent. Yield 71 mg (70%), R_f 0.50 (hexane–ethyl acetate, 5:1). Compound **V** was isolated as an oily substance containing minor *endo* esomer (ratio 7:1, according to the intensities of the MeO signals in the ^1H NMR spectrum). IR spectrum, ν, cm^{-1}: 1636, 1654, 1696, 1714, 3472. ^1H NMR spectrum, δ, ppm: 0.83 s (3H, CH_3), 1.13 s (3H, CH_3), 1.35 t (3H, CH_3, *J* = 7 Hz), 1.20–1.30 m (2H), 1.95 m (2H), 3.05 br.s (1H, OH), 3.20 br.s (1H, 1-H), 3.68 s (3H, OCH_3), 4.30 m (3H, 3-H, OCH_2), 5.10–5.30 m (2H) and 6.10–6.20 m (1H) ($CH=CH_2$). ^{13}C NMR spectrum, δ_C, ppm: 14.21 (CH_3), 19.83 (CH_3), 21.54 (CH_3), 25.31 (C^6), 29.02 (C^5), 49.64 (C^7), 50.86 (C^1), 54.87 (C^4), 59.66 (OCH_3), 60.76 (OCH_2), 80.06 (C^3), 116.48 and 134.99 ($CH=CH_2$), 140.37 (C^2), 151.69 ($C^{1'}$), 163.53 (CO_2). Found, %: C 68.42; H 8.41. $C_{16}H_{24}O_4$. Calculated, %: C 68.54; H 8.63.

The IR spectra were recorded on a UR-20 spectrophotometer from samples prepared as thin films. The ^1H and ^{13}C NMR spectra were obtained on a Bruker AM-300 spectrometer at 300 and 75.47 MHz, respectively, using $CDCl_3$ as solvent and TMS as internal reference. The optical rotation was measured on a Perkin–Elmer polarimeter. Thin-layer chromatography was performed on Silufol plates.

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