Reaction of myrtenal with dimethylamide of chloroacetic acid under the conditions of Darzens reaction

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3-[2-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)]-2-dimethylcarbamoyloxirane and the dimethylamide of 2-chloro-3-[2-(6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)]-3-(dimethylcarbamidomethyloxy)propionic acid were obtained by the reaction of myrtenal with dimethylamide of chloroacetic acid in the presence of NaH. The structures of the compounds obtained were confirmed by NMR, IR, UV, and CD spectroscopy and mass-spectrometry.

Key words: myrtenal, dimethylamide of chloroacetic acid, Darzens reaction; carbanions; NMR, IR, UV, and CD spectra.

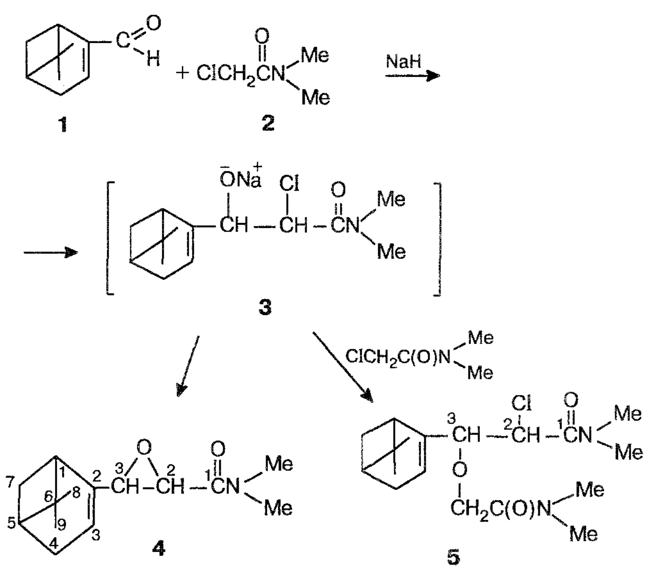
Reactions of carbanions generated from derivatives of halocarboxylic acids with carbonyl compounds (Darzens reaction) provide a convenient method for obtaining derivatives of 2,3-epoxycarboxylic acids.[1,2] In particular, amides of halocarboxylic acids react with aromatic aldehydes in the presence of strong bases to give amides of epoxycarboxylic acids.[3] However, the reactions of unsaturated aldehydes under these conditions have not been studied much.

In the present work we studied the reaction of myrtenal (**1**) with dimethylamide of chloroacetic acid (**2**) in the presence of NaH under Darzens reaction conditions (Scheme 1) resulting in epoxide **4** (yield 17 %) and ether **5** (yield 14 %). The formation of products **4** and **5** can be explained by competitive reactions of intra- and intermolecular alkylation of the intermediate alcoholate **3** formed through the addition of the carboanion generated from amide **2** by the action of NaH, to the carbonyl group of compound **1**.

The structures of compounds **4** and **5** were confirmed by spectral data. The ^1H NMR spectrum of epoxide **4** contains signals of protons of the three-membered ring at δ 3.45 and 3.48 ($^3J_{H,H}$ = 4.35 Hz), which imply their *cis*-orientation.[4,5] The ^{13}C NMR spectrum displays the signals of the C atoms of the epoxy group (δ 56.59 and 58.54, $J_{C,H}$ = 174.27 and 175.48 Hz, respectively).

The electron impact (EI) mass spectrum of ether **5** contains a molecular ion peak $[M]^+$ (m/z 356.1888), calculated value: M = 356.1887 (Δ = 0.0001). According to ^1H and ^{13}C NMR spectroscopy data, this compound is a mixture of two diastereomers in a 2.4 : 1.0 ratio.

Scheme 1



Experimental

^1H and ^{13}C NMR spectra of compounds **4** and **5** were recorded on a Bruker MSL-400 spectrometer at working frequencies of 400 and 100.6 MHz, respectively. The chemical shifts are given relative to $SiMe_4$. The EI mass spectrum of compound **5** was obtained on a MKh-1310 mass spectrometer. IR spectra were recorded on a UR-20 spectrophotometer in vaseline oil. UV spectra were obtained on a Specord M-40 spectrophotometer in MeCN. CD spectra were obtained on a Jasco 500A (Japan) spectropolarimeter in MeCN. Specific

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rotations were determined on a Polamat A polarimeter. Melting points were measured using a Boetius hot stage.

3-[2-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl]-2-dimethylcarbamoyloxirane (4). NaH (1.6 g) was added at 0 to −5 °C over a period of 1.5 h under argon to a mixture of myrtenal (10 g, 67 mmol) and the dimethylamide of chloroacetic acid (8.1 g, 67 mmol) in a small amount of dry ether. The mixture was stirred at ~20 °C for 4 h and kept overnight. Water (100 mL) was added, and the mixture was extracted with chloroform. The organic layer was separated and dried with $MgSO_4$. The solvent was evaporated, and the residue was distilled *in vacuo* to give 6.2 g (40 %) of a product, m.p. 114—118 °C (1.5 Torr). Storage of the distillate resulted in precipitation of crystalline compound **4**, m.p. 130.5—132 °C (Pr^iOH), yield 2.5 g (17 %), $[\alpha]_D^{20}$ +6.32 (*c* 5.6, CCl_4). Found (%): C, 71.32; H, 9.10; N, 6.12. $C_{14}H_{21}NO_2$. Calculated (%): C, 71.49; H, 8.94; N, 6.24. IR, ν/cm^{-1}: 1665 (C=O). UV, λ_{max}/nm: 218.2 (log ε 2.07). CD, λ_{max}/nm: 230 (Δε −42.5). ^1H NMR (CCl_4), δ: 0.75, 1.08, 1.27, 1.90—2.35, and 5.64 (pinene fragment); 2.81 and 3.07 ($CON(CH_3)_2$); 3.45 and 3.48 (CH—O—CH, *J* = 4.35 Hz). ^{13}C NMR (CCl_4—$CDCl_3$, 4 : 1), δ: 21.63 (q), 27.07 (q), 32.19 (t), 32.34 (t), 38.62 (s), 41.59 (d), 42.37 (d), 123.83 (d), and 142.21 (s) (pinene fragment); 35.69 and 36.77 (both q, $N(CH_3)_2$); 56.59 and 58.54 (both d, CH—O—CH).

Dimethylamide of 2-chloro-3-[2-(6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)]-3-(*O,N,N*-dimethylcarbamidomethyloxy)propionic acid (5). When the residue that was left after the synthesis of epoxide **4** but before distillation *in vacuo* was kept in a flask, its crystallization occurred to give 2.2 g (14 %) of compound **5**, m.p. 132.5—134 °C (Pr^iOH), $[\alpha]_D^{20}$ +4.34 (*c* 4.0, CCl_4). Found (%): C, 60.98; H, 8.15; N, 7.86. $C_{18}H_{29}N_2O_3Cl$. Calculated (%): C, 60.98; H, 8.15; N, 7.86. IR, ν/cm^{-1}: 1640 (C=O); 1655 (C=O). ^1H NMR (CCl_4; signals of two diastereomers (**A/B**) are present), δ: 2.87/2.84, 3.04/3.05, and 3.09 ($N(CH_3)_2$); 3.95/3.95 (CH_2O); 4.06/4.12 (CHCl); 4.39/4.24 (CHO). ^{13}C NMR (CCl_4—$CDCl_3$, 4 : 1; signals of two diastereomers (**A/B**) are present), δ: 22.07/21.74 (q), 26.93/27.18 (q), 32.32/32.02 (t), 32.41/32.50 (t), 38.94/38.53 (s), 41.46/41.24 (d), 42.82/42.44 (d), 127.19/128.30 (d), 143.45/143.12 (s) (pinene fragment); 55.54/55.02 (d, CHCl); 69.50/69.59 (t, CH_2O); 84.18/83.68 (d, CHO); 168.91/168.92 (C=O); 36.19/36.57, 36.71/36.96, 37.83/37.70, 38.10/38.00 (all q, 2 $CON(\underline{C}H_3)_2$).

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