Reaction of lithium acetylides with car-3-ene-2,5-dione

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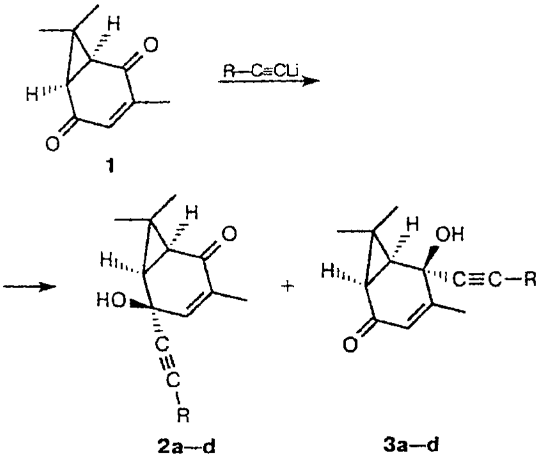
The reaction of car-3-ene-2,5-dione (1), an oxidation product of (+)-car-3-ene, with lithium acetylides proceeds stereospecifically, but not regioselectively, to give only mixtures of regioisomeric acetylenic alcohols with the *syn*-orientation of the hydroxy group.

Key words: (+)-car-3-ene, car-3-ene-2,5-dione, reaction with lithium acetylides; optical activity, stereochemistry.

Addition of lithium acetylides at the C=O bond is widely used in organic synthesis[1,2] as a convenient method for regiospecific and stereoselective formation of new C—C bonds.

In the present work, an interaction of lithium acetylides with optically active car-3-ene-2,5-dione (**1**) was studied. Initial lithium acetylides had been obtained *in situ* by the action of butyllithium on the corresponding alkynes in THF at 15 °C. Like substituted quinones,[3,4] compound **1** does not react with lithium acetylides regioselectively and yields mixtures of acetylenic alcohols.[2,3] Thus, dione **1** reacts with lithium phenylacetylide to give a mixture of 5-hydroxy-5-phenylethynylcar-3-en-2-one (**2a**) and 2-hydroxy-2-phenylethynylcar-3-en-5-one (**3a**) in the ratio of 2 : 3 in an overall yield of 89%.



R = Ph (**a**), Bu^n (**b**), C_5H_{11} (**c**), C_6H_{13} (**d**)

The structures of compounds **2a** and **3a** were determined from ^{13}C and ^1H NMR spectral data. Two sets of signals with an intensity ratio of 2 : 3 are observed in the ^{13}C NMR spectrum of the mixture of the isomers. The minor component corresponds to the structure of **2a** with retention of the carbonyl group at the C(2) atom. The conjugation with this group results in shielding the C(3) atom (a singlet with δ 133.8) and deshielding the C(4) atom (a doublet with δ 144.6). A reverse sequence of the signals of the carbon atoms at the double bond is observed in the predominant component of the spectrum (isomer **3a**): a singlet of the C(3) atom (δ 161.1) and a doublet of the C(4) atom (δ 126.1). A similar result was obtained from ^1H NMR spectra: the singlet of the proton at the double bond is observed at δ 6.48 for compound **2a**, whereas it was observed at δ 5.78 for isomer **3a**. The configuration of the hydroxy group was determined from measuring the nuclear Overhauser effect in ^1H NMR spectra. An increase in intensity of the signal of the OH group upon irradiation of the methyl protons of the cyclopropane fragment suggests the *syn*-orientation of the hydroxy group in isomers **2a** and **3a**.

Analogously, a reaction of dione **1** with lithium 1-hexynylide gives isomers **2b** and **3b** in the ratio of 1 : 3. The signals in the range of δ 1.80 and 6.27 in the ^1H NMR spectrum of compound **2b** correspond to the methyl group at the C(3) atom and to the proton at the C(4) atom, whereas these signals for isomer **3b** are observed at δ 2.08 and 5.80, respectively. Similar differences were also found for the pair of isomers, **2c** and **3c**, which resulted in the same ratio from a reaction of dione **1** with lithium 1-heptynylide. An interaction of compound **1** with lithium 1-octynylide led to a mixture of isomers **2d** and **3d** in the ratio of 1 : 1.

The products synthesized are rather unstable: they decompose under heating and when chromatographed on a column with silica gel. However, they were isolated in the individual state by column chromatography with phlorisil. Alcohols containing the hydroxy group at the C(5) atom have a positive optical rotation angle, while their isomers with the OH group at the C(2) atom have a negative angle.

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Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Tesla BS-567 B spectrometer (100 MHz) and a Bruker AM-300 spectrometer (75 MHz), respectively ($CDCl_3$, with tetramethylsilane as the internal standard). IR spectra were recorded on a UR-20 instrument (Vaseline oil), and UV spectra were recorded on a Specord M-400 spectrometer. Optical rotation was measured on a Perkin—Elmer 141 instrument. Preparative separation was performed on columns with phlorisil (100/200 mesh) using a hexane—ether mixture as an eluent. TLC was performed on Silufol plates.

Car-3-ene-2,5-dione (1). (+)-Car-3-ene (45.3 g, 330 mmol; $[\alpha]_D^{20}$ +16° (*c* 1.0, $CHCl_3$)) and cobalt stearate (1.13 g, 2 mmol) were placed in an autoclave and, after the latter was hermetically sealed, O_2 (20 atm) and N_2 (40 atm) were forced. Then the reaction mixture was dissolved in 300 mL of ether, washed in succession with a cold $NaHCO_3$ solution and a saturated NaCl solution, and dried with $MgSO_4$. After the solvent was removed, a mixture of products of (+)-car-3-ene oxidation (44.8 g) was obtained that contained 46% diketone **1**. After vacuum distillation, product **1** (13.0 g) was isolated, b.p. 88—92 °C (3 Torr), m.p. 100—101 °C (from EtOH). $[\alpha]_D^{20}$ −15° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 1625, 1665. UV (EtOH), λ_{max}/nm (log ε): 226 (3.95), 242 (4.01). ^{1}H NMR, δ: 1.33 (s, 6 H, 2 Me); 1.95 (br.s, 3 H, Me); 2.33 (m, 2 H, 2 CH); 6.50 (br.s, 1 H, C=CH). ^{13}C NMR, δ: 39.9 (d, C(1)); 195.1 (s, C(2)); 150.1 (s, C(3)); 137.7 (d, C(4)); 194.4 (s, C(5)); 39.1 (d, C(6)); 33.6 (s, C(7)); 15.5 (q, C(8)); 16.2 (q, C(9)); 29.1 (q, C(10)).

Reactions of lithium acetylides with car-3-ene-2,5-dione. A 2.7 *M* Bu^{n}Li solution (1.2 mL) in hexane was added to a solution of phenylacetylene (0.30 g, 3 mmol) in 3 mL of anhydrous THF with stirring and cooling to −15 °C. The reaction mixture was stirred at the same temperature for 20 min and then a solution of diketone **1** (0.50 g, 3 mmol) in 5 mL of anhydrous THF was added. The resulting solution was stirred at −15 °C for 2 h, and 2 mL of MeOH was added and heated to 0 °C. A 5% NH_4Cl solution (6 mL) was added at this temperature and stirring was continued for an extra 15 min with increasing temperature to ~20 °C. Then 3 mL of water was added, and the reaction mixture was extracted with ether. The extract was washed with water, dried with $MgSO_4$, and concentrated *in vacuo*. A mixture of isomers **2a** and **3a** (0.73 g, 89%, in the ratio of 2 : 3) was isolated. The isomers were separated by column chromatography with phlorisil.

5-Hydroxy-5-phenylethynylcar-3-en-2-one (2a). $[\alpha]_D^{20}$ +186.1° (*c* 1.0, EtOH). IR, ν/cm^{-1}: 1643, 3300. UV (EtOH), λ_{max}/nm (log ε): 232 (4.28). ^{1}H NMR, δ: 1.26 (s, 3 H, Me); 1.34 (s, 3 H, Me); 1.80 (s, 3 H, Me); 1.87 (d, 1 H, CH, $J_{H(1)H(6)}$ = 7.6 Hz); 2.16 (dd, 1 H, CH, $J_{H(6)H(1)}$ = 7.6 Hz, $J_{H(6)H(4)}$ = 1.5 Hz); 2.61 (s, 1 H, OH); 6.48 (d, 1 H, C=CH, $J_{H(4)H(6)}$ = 1.5 Hz); 7.4—7.5 (m, 5 H, Ph). ^{13}C NMR, δ: 37.4 (d, C(1)); 197.8 (s, C(2)); 133.8 (s, C(3)); 144.6 (d, C(4)); 64.8 (s, C(5)); 36.1 (d, C(6)); 28.1 (s, C(7)); 16.7 (q, C(8), C(9)); 19.6 (q, C(10)); 85.6 (s, C(11)); 92.1 (s, C(12)); 123.1 (s, C(13)); 132.5 (d, C(14), C(18)); 129.2 (d, C(15), C(17)); 129.5 (d, C(16)).

2-Hydroxy-2-phenylethynylcar-3-en-5-one (3a). $[\alpha]_D^{20}$ −298.8° (*c* 1.0, EtOH). IR, ν/cm^{-1}: 1620, 3240. UV (EtOH), λ_{max}/nm (log ε): 239 (4.32). ^{1}H NMR, δ: 1.26 (s, 3 H, Me); 1.31 (s, 3 H, Me); 2.20 (s, 3 H, Me); 1.83 (dd, 1 H, CH, $J_{H(6)H(1)}$ = 7.8 Hz, $J_{H(6)H(4)}$ = 1.2 Hz); 2.22 (d, 1 H, CH, $J_{H(1)H(6)}$ = 7.8 Hz); 2.41 (s, 1 H, OH); 5.78 (d, 1 H, C=CH, $J_{H(4)H(6)}$ = 1.2 Hz); 7.4—7.5 (m, 5 H, Ph). ^{13}C NMR, δ: 36.7 (d, C(1)); 67.2 (s, C(2)); 161.1 (s, C(3)); 126.1 (d, C(4)); 197.5 (s, C(5)); 38.6 (d, C(6)); 28.2 (s, C(7)); 16.2 (q, C(8), C(9)); 29.9 (q, C(10)); 85.3 (s, C(11)); 92.1 (s, C(12)); 123.1 (s, C(13)); 132.5 (d, C(14), C(18)); 129.2 (d, C(15), C(17)); 129.5 (d, C(16)).

Reactions of lithium acetylides $R-C\equiv C-Li$ (R = Bu, C_5H_{11}, C_6H_{13}) with carenedione **1** were carried out similarly. Products **2b,c,d—3b,c,d** were isolated by column chromatography with phlorisil.

5-Hexynyl-5-hydroxycar-3-en-2-one (2b). $[\alpha]_D^{20}$ +88.0° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 1670, 3440. UV (EtOH), λ_{max}/nm (log ε): 206 (4.33), 254 (4.20). ^{1}H NMR, δ: 0.91 (s, 3 H, Me); 1.22 (s, 3 H, Me); 1.28 (s, 3 H, Me); 1.36—1.60 (m, 4 H, 2 CH_2); 1.80 (s, 3 H, Me); 1.90 (m, 1 H, CH); 1.97 (m, 1 H, CH); 2.23 (m, 2 H, $C\equiv C-CH_2$); 2.66 (s, 1 H, OH); 6.27 (s, 1 H, C=CH).

2-Hexynyl-2-hydroxycar-3-en-5-one (3b). $[\alpha]_D^{20}$ −107.8° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 1650 (C=O); 3350 (OH). UV (EtOH), λ_{max}/nm (log ε): 236 (4.06). ^{1}H NMR, δ: 0.91 (s, 3 H, Me); 1.23 (s, 3 H, Me); 1.25 (s, 3 H, Me); 1.34—1.60 (m, 4 H, 2 CH_2); 1.80 (m, 1 H, CH); 2.0 (m, 1 H, CH); 2.08 (s, 3 H, Me); 2.22 (m, 2 H, $C\equiv C-CH_2$); 2.48 (s, 1 H, OH); 5.80 (s, 1 H, C=CH).

5-Heptynyl-5-hydroxycar-3-en-2-one (2c). $[\alpha]_D^{20}$ +18.4° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 1672 (C=O); 3410 (OH). UV (EtOH), λ_{max}/nm (log ε): 210 (4.08), 239 (4.05). ^{1}H NMR, δ: 0.97 (s, 3 H, Me); 1.24 (s, 3 H, Me); 1.27 (s, 3 H, Me); 1.30—1.68 (m, 7 H, 3 CH_2, CH); 1.80 (s, 3 H, Me); 1.91 (m, 1 H, CH); 2.25 (t, 2 H, $C\equiv C-CH_2$); 2.68 (s, 1 H, OH); 6.27 (s, 1 H, C=CH).

2-Heptynyl-2-hydroxycar-3-en-5-one (3c). $[\alpha]_D^{20}$ −52.3° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 1665 (C=O); 3400 (OH). UV (EtOH), λ_{max}/nm (log ε): 230 (4.21). ^{1}H NMR, δ: 0.96 (s, 3 H, Me); 1.23 (s, 3 H, Me); 1.25 (s, 3 H, Me); 1.28—1.66 (m, 6 H, 3 CH_2); 1.70—2.16 (m, 2 H, 2 CH); 2.08 (s, 3 H, Me); 2.22 (m, 2 H, $C\equiv C-CH_2$); 2.40 (s, 1 H, OH); 5.77 (s, 1 H, C=CH).

5-Hydroxy-5-octynylcar-3-en-2-one (2d). $[\alpha]_D^{20}$ +59.3° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 1670, 3415. UV (EtOH), λ_{max}/nm (log ε): 215 (3.97), 218 (3.96), 236 (3.99). ^{1}H NMR, δ: 0.90 (s, 3 H, Me); 1.22 (s, 3 H, Me); 1.26 (s, 3 H, Me); 1.50 (m, 8 H, 4 CH_2); 1.80 (s, 3 H, Me); 1.90 (m, 1 H, CH); 2.10 (m, 1 H, CH); 2.26 (m, 2 H, $C\equiv C-CH_2$); 2.62 (s, 1 H, OH); 6.30 (s, 1 H, C=CH).

2-Hydroxy-2-octynylcar-3-en-5-one (3d). $[\alpha]_D^{20}$ −119.3° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 1665, 3400. UV (EtOH), λ_{max}/nm (log ε): 238 (4.16). ^{1}H NMR, δ: 0.97 (s, 3 H, Me); 1.23 (s, 3 H, Me); 1.25 (s, 3 H, Me); 1.25—1.58 (m, 8 H, 4 CH_2); 1.82 (m, 1 H, CH); 1.90 (m, 1 H, CH); 2.08 (s, 3 H, Me); 2.29 (m, 2 H, $C\equiv C-CH_2$); 2.38 (s, 1 H, OH); 5.76 (s, 1 H, C=CH).

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