Asymmetric Induction in Addition Reactions of Carbanions to Levoglucosenone

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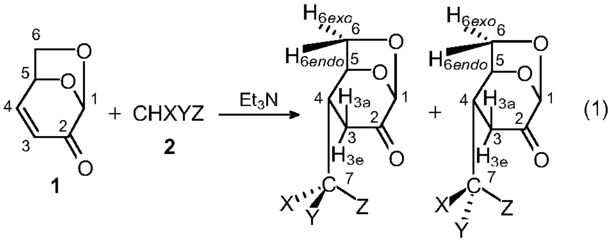
Michael addition of a series of carbanions to levoglucosenone, giving mixtures with different epimer ratios depending on the nature of the carbanion, has been studied.

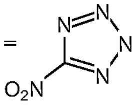
Carbanion addition to levoglucosenone has so far only been investigated for a few examples.[1,2] The present communication is dedicated to those aspects of the addition stereochemistry which have scarcely been touched upon in previous work.

Levoglucosenone **1**, usually obtained by cellulose pyrolysis,[3] is optically active, its molecule bearing two asymmetric centres (C1 and C5) whose configurations are "inherited" from the cellulose macromolecule. During carbanion addition to **1** in general two new asymmetric centres, C4 and C7, appear [reaction (1)]. It is clear that the addition to C4 proceeds stereoselectively, namely, from the side opposite to the 1,6-anhydro-bridge (this is true both for carbanions[1,2] and for *O*- and *S*-nucleophiles;[3,4] in our work[5] it was shown that the same is true for *N*-nucleophiles, *i.e.*, azoles). Thus, in the case of carbanions the formation of two epimers on C7 is possible, reaction (1).



1 **2** **3a–d** (1)

a X = H; Y = NO$_2$; Z = COOEt
b X = Me; Y = NO$_2$; Z = COOEt
c X = CH$_2$CH$_2$COOEt; Y = NO$_2$; Z = COOEt
d X = H; Y =



; Z = COPh

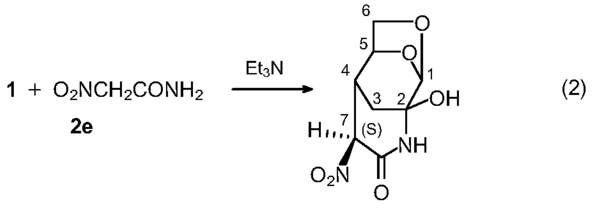
The question of the epimeric ratio, *i.e.*, asymmetric induction in the addition process, is the focus of attention in this work.

In ref. 1 the formation of a 1:1 epimeric mixture in cyanoacetic ester (NCCH$_2$COOEt) addition to **1** was reported. In the present work some more compounds have been investigated in order to obtain a fuller picture: ethyl nitroacetate **2a**, ethyl α-nitropropionate **2b**, diethyl α-nitroglutarate **2c** (obtained from **2a** and ethyl acrylate according to ref. 6), 5-nitro-2-phenacyltetrazole **2d** (obtained according to ref. 7) and nitroacetamide **2e**. The procedure involved (see below) significantly increases the yield of adducts **3a–c**.[2] The results obtained for **2a–d** are presented in Table 1 (epimeric ratio was determined by ^{1}H NMR spectroscopy).

The low degree of asymmetric induction, *i.e.* epimer ratio close to 1 is worthy of attention. This is correct both for similar compounds **3a–c** and for different compound **3d**; both for **3a,d** where an acidic proton enables epimerization and for **3b,c** where it is impossible.

Table 1 Yield of adducts **3a–c** from acids **2a–d**.

C–H acid	Product (total yield in %; epimer ratio)
2a	**3a** (75; 1:1)
2b	**3b** (86; 4:3)
2c	**3c** (83; 4:3)
2d	**3d** (64; 4:3)



4e (2)

Quite another event takes place in the reaction of **1** with **2e**. In this case the addition is accompanied by cyclization and the single product **4e** is formed in 62% yield, reaction (2).

The assumption of (*S*)-configuration at C7 is based on the fact that $J_{\mathrm{H4,H7}} = 0$. Thus, in reaction (2) new asymmetric centres, C4, C7 and C2, are formed and all of them with complete stereochemical control.†

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† *General procedure*: To a solution of **2a–e** (5 mmol) in 3 ml of solvent (CHCl$_3$ for **2a–c** and MeCN for **2d,e**, heated to 40–50 °C), 10% mol Et$_3$N was added, then a solution of **1** (5 mmol) in 5 ml of the same solvent was added dropwise during 30–40 min. The reaction was allowed to continue for 48 h, then the reaction mixture was washed with dilute HCl, dried over CaCl$_2$ and the solvent was evaporated. Adducts were obtained as yellow oils [except **4e**, which formed colourless crystals, m.p. 194–197 °C (decomp.)].

^{1}H NMR spectra of **3a–c** were presented in ref. 2; their ^{13}C NMR spectra and also ^{1}H NMR spectra of **3d** and **4e** are presented below.

3a: 13.73 (Me); 32.77, 33.50 (C3); 41.33, 41.43 (C4); 63.79 (CH$_2$); 67.68, 67.95 (C6); 73.15, 73.24 (C5); 87.98, 88.56 (C7); 101.40 (C1); 163.01, 163.22 (C=O ester); 196.34, 196.66 (C2).

3b: 12.93, 13.10 (Me ester); 18.70, 19.71 (Me); 32.02, 32.41 (C3); 43.66, 44.13 (C4); 62.68, 63.11 (CH$_2$); 68.21, 68.49 (C6); 72.33 (C5); 94.05, 94.32 (C7); 100.11, 100.24 (C1); 165.31, 166.03 (C=O ester); 197.79, 197.97 (C2).

3c: 13.25, 13.60, 13.97 (Me ester); 26.50, 26.62, 28.79, 29.70 (CH$_2$CH$_2$); 32.51, 32.85 (C3); 60.98, 61.02, 63.25, 63.66 (CH$_2$ ester); 68.49, 69.06 (C6); 72.19, 72.32 (C5); 95.81, 96.20 (C7); 100.30, 100.82 (C1); 165.38, 171.20, 171.43 (C=O ester); 196.79, 197.44 (C2).

3d: ^{1}H NMR: 2.24, 2.42 (dm; H3e; J = 18.1 Hz); 3.02, 3.18 (dd; H3a; J = 18.1 Hz, J = 8.5 Hz); 3.67–3.79 (m; H4); 4.02, 3.93 (dd; H6$_{exo}$; J = 8.0 Hz, J = 5.6 Hz); 4.37, 4.34 (dd; H6$_{endo}$; J = 8.0 Hz, J = 1.1 Hz); 4.94, 4.43 (br.d; H5; J = 5.6 Hz); 4.99, 5.05 (s; H1); 7.42, 7.32 (d; H7; J = 9.6 Hz and J = 11.1 Hz); 7.5–7.8 (m; Ph, *m*- and *p*-); 8.21, 8.09 (dd; Ph, *o*-; J = 8.1 Hz; J = 1.0 Hz) (chemical shifts for major epimer are shown first).

4e: ^{1}H NMR: 2.24 (dm; H3e; J = 13.2 Hz); 2.36 (dd; H3a; J = 13.2 Hz, J = 3.5 Hz); 2.83 (m; H4); 3.83 (dd; H6$_{exo}$; J = 8.0 Hz, J = 4.8 Hz); 4.15 (br.d; H6$_{endo}$; J = 8.0 Hz); 4.81 (m; H5); 4.98 (d; H1; J = 1.8 Hz); 5.31 (br.s; H7); 5.8–5.95 (br.s); 7.15–7.25 (br.s) (OH, NH). ^{13}C NMR: 29.55 (C3); 38.82 (C4); 68.15 (C6); 76.26 (C5); 82.80 (C2); 84.36 (C7); 104.09 (C1).

Spectra of **3a–c** were recorded in CDCl$_3$ and those of **3d** and **4e** in (CD$_3$)$_2$CO.

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