## DIASTEREOSELECTIVE REACTIONS OF SELENO-ACETALS

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<u>Summary</u>: The diastereoselective refunctionalization of the seleno-acetals <u>1b</u> into various seleno-ethers <u>3b</u> is reported. The diastereomer ratio of the products <u>3b</u> reflects the thermodynamic ratio of the intermediate  $\alpha$ -phenylseleno-lithium compounds <u>7</u> at -78 °C.

We studied previously <sup>1)</sup> the stereochemical aspects of the bromine/lithium exchange of the diastereotopic bromine atoms in <u>1a</u> to generate the carbenoids <u>2a</u>, as well as that of the subsequent C-C-bond forming reactions of these carbenoids. Here, the configurational stability of the intermediary carbenoid <u>2a</u> is of prime importance. Our results suggested <sup>1)</sup> that the carbenoids <u>2a</u> are configurationally stable at -120 °C. Hence, the product ratio of <u>3a</u> is determined in the bromine/lithium exchange step <u>1a</u> + <u>2a</u>. The related seleno-acetals <u>1b</u> might undergo similar stereoselective transformations, because it is known that seleno-acetals exchange one selenyl group for lithium, when treated at low temperatures with n-butyllithium <sup>2)</sup>. The resulting  $\alpha$ -phenylseleno-lithium compounds add to a variety of carbon- and heteroatom-electrophiles in good yields <sup>3)</sup>. For this reason we investigated the stereoselectivity of the <u>1b</u> + <u>2b</u> + <u>3b</u>

transformations.  $Me_3SiO X$  <u>n-BuLi</u>  $Me_3SiO X$  <u>Electrophile, E<sup>+</sup> Me\_3SiO X</u>



The phenylseleno-acetal <u>6</u> was prepared <sup>4)</sup> from the aldehyde <u>4</u> via the acetal <u>5</u>. Selenium/lithium exchange was effected with one equivalent of n-butyllithium in ether over 20 min at -78 °C. The resulting <u>7</u> was quenched with cyclohexanone to give 71 % of <u>8</u> as a 90 : 10 mixture of diastereomers. The  $\alpha$ -phenylseleno-lithium intermediate could also be trapped by other electrophiles, cf. table.

The diastereoselectivity observed does not depend to a significant extent on the nature of the electrophile. This could be interpreted in terms of

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configurationally stable organolithium compounds  $\underline{7}$  being generated by selective exchange of the diastereotopic seleno groups in 6. However, this would be in contrast to recent findings of A. Krief 5 and H.J. Reich 6 who showed that tertiary  $\alpha$ -phenylseleno-lithium compounds are configurationally labile and epimerize within minutes at -78 °C. The following set of experiments shows that this applies equally to the secondary  $\alpha$ -phenyl-seleno-lithium compounds 7.

Experiment (1)



Experiment (2)



For the sake of the argument, let us assume that the organolithium compounds  $\underline{7}$  be configurationally stable at -78 °C. Then, the diastereomer ratio of the acetone adducts from the first experiment would reflect the preference for the exchange of one of the diastereotopic phenylseleno groups in  $\underline{6}$ . Likewise in the second experiment the diastereomer ratio of  $\underline{11}$  would reflect a similar preference for the exchange of the diastereotopic methyl-seleno groups in  $\underline{9}$  as the congruent A : B and C : D ratios suggest. Ex-

Me₃SiO SePh	Electrophile, E*	Me <sub>3</sub> SiO SeF	h
	- 78 °		E
Electrophile	Yield	ds	Adduct
Acetone	93 %	91 : 9 <sup>a,b</sup>	Me <sub>3</sub> SiQ SePh
Cyclopentanone	58 %	85 : 15 <sup>ª</sup>	Me <sub>3</sub> SiO SePh
2-Cyclohexenone	89 %	(51 + 39) : (6 + 4) <sup>b</sup>	Me <sub>3</sub> SiO SePh
i-Butyraldehyde	87 %	(63 + 30) : (5 + 2) <sup>b</sup>	Me <sub>3</sub> SiO SePh
CH₃OCOCI	82 %	90 : 10 <sup>a</sup>	
Me2tBuSiOSO2CF3	96 %	93 : 7 <sup>b</sup>	Me <sub>3</sub> SiO SePh
Me <sub>3</sub> SiOSO <sub>2</sub> CF <sub>3</sub>	77 %	93 : 7 <sup>b</sup>	SiMe <sub>3</sub>

## TABLE : Addition of the α-Phenylseleno-Lithium Compounds 7 to Electrophiles

The diastereomer ratios have been determined by: a) <sup>13</sup>C-NMR, b) GC. The relative configuration of the diastereomers has not yet been assigned

change of the remaining methylseleno group in <u>11</u> for lithium should now generate the  $\alpha$ -phenylseleno-lithium compounds <u>7</u> with an "inverted" diastereomer ratio, so that after addition to acetone A and B would be expected to arise in the inverted 1 : 9 ratio.

Contrary to this expectation, experiments (1) and (2) gave identical product ratios. This provides evidence that at least in experiment (2) either or both of the organolithium intermediates <u>10</u> or <u>7</u> must have epimerized. By inference we are led to conclude that also in experiment (1) and all the results reported in the table the epimeric organolithium compounds <u>7</u> had equilibrated before they added to an electrophile. The essentially constant diastereomer ratios reported in the table therefore reflect the thermodynamic ratio of the diastereomeric lithium compounds <u>7</u> (9 : 1), because probably the rate by which the epimers of <u>7</u> are trapped by the electrophiles is faster than the rate of epimerization of <u>7</u>. This would be a case in which the Curtin-Hammett principle does not apply. If in turn the rate of trapping of <u>7</u> by electrophiles would be slower than the rate of epimerization, different diastereomer ratios should result (the Curtin-Hammett case). So far we have found one such example, the "slow" reverse Brook rearrangement 7,8 of 7 with an onset at -40 °C leading to the silyl derivatives 12.



This rearrangement is intramolecular according to a cross-over experiment using 1b (with R = t-Bu and a  $t-Bu-Me_2Si-protective group)$  as the second component. The diastereomer ratio of the silyl derivatives 12 from the reverse Brook rearrangement (66 : 34) differs from that obtained when trapping 7 at -78 °C with TMS-triflate (93 : 7). The former ratio is interpreted to reflect the kinetic diastereoselection in the rearrangement process of two rapidly equilibrating epimers of 7.

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## References

- R.W. Hoffmann, M. Bewersdorf, K. Ditrich, M. Krüger, R. Stürmer, Angew. Chem. <u>100</u> (1988) 1232; Angew. Chem., Int. Ed. Engl. <u>27</u> (1988) 1176.
   A. Krief, W. Dumont, M. Clarembeau, G. Bernard, E. Badaoui, Tetrahedron
- 45 (1989) 2005; A. Krief, W. Dumont, M. Clarembeau, E. Badaoui, Tetrahedron 45 (1989) 2030.
- 3) A. Krief, Tetrahedron 36 (1980) 2531.
- 4) M. Clarembeau, A. Cravador, W. Dumont, L. Hevesi, A. Krief, J. Lucchetti, D. Van Ende, Tetrahedron <u>41</u> (1985) 4793.
  5) A. Krief, G. Evrard, E. Badaoui, V. De Beys, R. Dieden, Tetrahedron
- Letters, submitted.
- 6) M. D. Bowe, H.J. Reich, Abstr. ORGN 238, 198 Meeting Amer. Chem. Soc. (1989).
- 7) D.A. Evans, J.M. Takacs, K.M. Hurst, J. Am. Chem. Soc. <u>101</u> (1979) 371; J. Mora, A. Costa, Tetrahedron Lett 25 (1984) 3493; M. Braun, H. Mahler, Angew. Chem. 101 (1989) 948; Angew. Chem., Int. Ed. Engl. 28 (1989) 896.
- 8) E.J. Bures, B.A. Keay, Tetrahedron Lett. 28 (1988) 5965.

Representative data for the major diastereomer of 8: <sup>1</sup>H-NMR (300 MHz,  $CDCl_3$ ):  $\delta = 0.15$  (s, 9H), 0.66 (d, J = 6.8 Hz, 3H), 0.75 (d, J = 6.8 Hz, 2H) 3H), 1.43 - 1.71 (m, 11H), 1.79 (ddd, J = 14.6, 10.5, and 4.1 Hz, 1H), 2.10 (ddd, J = 14.7, 8.4, and 3.9 Hz, 1H), 2.93 (s, 1H), 3.09 (dd, J =10.5 and 3.8 Hz, 1H), 3.90 (ddd, J = 8.3, 4.2, and 3.8 Hz, 1H), 7.23 – 7.27 (m, 3H), 7.56 – 7.61 (m, 2H); <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.43, 15.3, 19.5, 21.7, 22.2, 25.7, 30.1, 34.7, 37.4, 60.9, 73.0, 75.5, 127.3, 129.1, 131.1, 133.9.

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