On the Carbocyclization of ω -Styrenylbenzyllithiums

Alain Krief,* Bruno Remacle, Willy Dumont

Laboratoire de Chimie Organique de Synthèse, Departement of Chemistry, Facultés Notre Dame de la Paix, 61 rue de Bruxelles, B5000 Namur, Belgium. Fax (0032) 8172 4536; E-mail: alain.krief@fundp.ac.be

Received 15 March 1999

Dedicated with warm affection and deep admiration to Professor L. Ghosez at the occasion of his 65th Birthday

Abstract: ω -Styrenylbenzyllithiums readily available from the corresponding ω -styrenylbenzyl selenides and butyllithiums provide after methanolysis 1-aryl-2-benzyl cyclopentanes with very high stereocontrol. The compound bearing these two groups in *trans*-position is produced, when the reaction is carried out in THF at -78 °C or in ether at -100 °C whereas its stereoisomer is generated if the reaction is performed in ether at 0 °C. We proved that these reactions occur under kinetic control.

Key words: arylcyclopentanes, benzyllithiums, diastereoselection, carbocyclisation

A few years ago we reported that the ω -alkenylbenzyllithium **2a** (R = H, Scheme 1) possesses a very high propensity to rearrange to cyclopentylmethyllithium **3a** which after hydrolysis led to the corresponding 1,2-dimethyl-1phenyl cyclopentane **4a** with almost complete stereocontrol depending upon the nature of the solvent and the temperature used (**3a'** and **4a'** in ether at 20 °C, **3a''** and **4a''** in THF at -78 °C).^{1a} The reaction proved to be quite general since related compounds whose C,C double bond bears a thiophenyl group (R = SPh, Scheme 1) behave similarly.^{1b}

Cyclization even takes place with the ω -alkenylbenzyllithium **1c** bearing a methyl substituent on the C,C double bond,^{1c} but instead leads to the cyclopent[a]indene **5c** in pentane (20 °C, 24 h; **4'/5/7** ratio 3/97/0 by GC) and to 1,2-dimethyl-1-phenyl-cyclohexane **7c** soiled with some of **4c** and **5c** in THF (-78 °C, 0.5 h; 46% yield; **4''/5/7** ratio 15/22/63 by GC).



Scheme 1

Synlett 1999, No. 07, 1142–1144 ISSN 0936-5214 © Thieme Stuttgart \cdot New York

We wanted to get an insight into the intimate mechanism of such reactions in order to better understand the reasons for such a discrepancy between the different results cited above and decided to study the reactivity of the benzylse-lenide **1d**, bearing a phenyl substituted C,C double bond towards alkyllithiums.^{2,3}

Benzylselenide 1d was expected to be the precursor of both benzyllithiums (2d and 3d resulting respectively from the C-Se bond cleavage and the carbolithiation reaction) which should possess carbanions of related stability and therefore should be particularly prone to equilibrate.

2,7-Diphenyl-2-(methylseleno)-heptene **1d**, prepared from 1,1-bis (methylseleno)-1-phenylethane, *n*-BuLi ^{4a} and 5-bromo-1-phenyl-pent-1-ene, leads, on reaction with *n*-BuLi in THF at -78 °C, and methanolysis at that temperature, to the cyclopentane derivative **4d** as a 3/97 mixture of stereoisomers **4'd/4''d** (Scheme 1, Table, entry a). The same reaction is still effective in ether at -78 °C but it requires the use of the more reactive *s*-BuLi ^{4b} to cleave the C,Se bond and provides the same mixture of stereoisomers but with a lower stereoselectivity (Scheme 1, Table, entry b, compare to entry a).

Most of the reactions have been carried on a (1/1) mixture of Z/E isomers of **1d**. In few cases, we have used a starting material highly enriched in one or the other stereoisomer and have not observed significant change on the **4'd/4''d** ratio of stereoisomers.⁵

We have screened, in order to control more efficiently its stereochemical outcome, the effect of the temperature on

Table Carbocyclization of ω-stryrenyl benzyllithiums

Entry	Conditions	4d yield % (4'/4" ratio)
a	(i) <i>n</i> -BuLi, THF, -78°C, 1h (ii) MeOH, -78°C	83 (3/97)
b	(i) s-BuLi, ether, -78° C, 1h (ii) MeOH, -78° C	70 (33/67
c	(i) <i>s</i> -BuLi, ether, 0°C, 1h (kk) MeOH, 0°C	72 (98/2)
d	(i) s-BuLi, ether, -45° C, 1h (ii) MeOH, -45° C	80 (90/10)
e	(i) s-BuLi, ether, -65° C, 1h (ii) MeOH, -65° C	65 (44/56)
f	(i) s-BuLi, ether, -100°C, 1h (ii) MeOH,	70 (8/92)
	-100°C	
g	(i) <i>s</i> -BuLi, ether, -100°C, 1h (ii) MeOH, 0°C	70 (4/96)
ĥ	(i) n-BuLi, THF, 0°C, 1h (ii) MeOD	75 (27/73)
i	(i) <i>n</i> -BuLi, THF, –78°C, 1h (ii) –78°C to 0°C,	60 (26/74)
	1h, (iii) MeOD, 0°C	

the reaction performed in ether. We unexpectedly found that it is possible to produce in ether either the almost pure cyclopentane stereoisomer **4'd** or **4''d** selectively by performing the reaction at 0 °C (Table, entry c) or at -100 °C (Table, entry f).

We also found that the ratio of stereoisomers changes continuously between 0 °C and -100 °C (Table, entries b-f) and that the significant change occurs around -65 °C (Table, entry e).

These reactions occur under kinetic control in the whole range of temperature studied from -100 °C to 0 °C since the same ratio of stereoisomers is obtained when the reaction performed at -100 °C and is then quenched with deuteromethanol either at that temperature or at 0 °C (Table entries f, g).

Reactions performed in THF do not exhibit similar behavior since epimerisation takes place when the reaction carried out at -78 $^{\circ}$ C is heated to 0 $^{\circ}$ C prior to methanolysis (Table, entry i).

Furthermore we proved that the reaction proceeds under kinetic control in THF at -78 °C (Table, entry a). Indeed the benzyllithium **3'd**, prepared in THF at -78 °C, from benzylselenide **8'd** and *n*-butyllithium does not isomerize to **3''d** since **4'd** is obtained almost exclusively after methanolysis (-78 °C, 0.5h then MeOH, -78 °C, Scheme 2).⁶

The benzylselenide **8'd** required for this study was easily prepared (Scheme 3) by quenching **3'd** (prepared from **1d** and *t*-butyllithium in pentane)^{4c,7} with dimethyldiselenide (1 equiv. MeSeSeMe, 20 °C, 1 h, 32% yield). The newly formed benzylselenide **8d** is a stereoisomeric mixture in which the *cis*-stereoisomer at the ring junction predominates (**8'd/8''d** :74/26) but each stereoisomer is an epimeric mixture at the benzyl site where the methylseleno moiety has been introduced (**8'd** α ; 77/23; **8''d** α/β ; 74/26).

We also prepared, for control experiments the *trans*stereoisomer **8''d** by performing the two consecutive reactions in THF ((i) 1 equiv. *n*-BuLi, THF, -78 °C, 0.5 h, (ii) 1 equiv. MeSeSeMe, THF, -78 °C to 20 °C; 73% yield, **8''d/8'd** 98/2, **8''d** α/β : 87/13) and have unambiguously assessed the stereochemistry of the major stereoisomer **8''d**_a (Scheme 3) by X-ray crystallography.

T selenides **8'd** and **8''d** have been also prepared in a more expedite way by reacting **1d** with a catalytic amount of BuLi (Scheme 4) :

in ether ((i) 0.2 equiv. *t*-BuLi, ether, 0 °C, 0.1h (ii) 0° to 20 °C, 24 h; 8d 56% yield, 8'd/8"d 72/23; 8'd a/b: 62/38; 8"d a/b: 55/45) or

in THF ((i) 0.2 equiv. *n*-BuLi, THF, -78 °C, 0.5h (ii) 20 °C, 24h, 8d, 80% yield, 8'd/8"d 18/82; 8'd α/β :62/ 38; 8"d α/β : 52/48).



Scheme 2



Scheme 3



Scheme 4

These results led us to assume that the newly formed primary benzylic carbanion 3d is able to cleave, in both solvents used, the C-Se bond of the open chain tertiary benzylic derivative 1d, producing simultaneously the benzylic selenide 8d and the open chain tertiary-benzyllithium 2d which perpetuates the cycle until 1d has completely disappeared (Scheme 4). Related isomerizations have been recently described.⁸

Work is in progress to determine the behavior of related derivatives bearing different substituent on the C,C double bond.

Acknowledgement

Authors thanks the FRIA (Fonds de Recherche pour l'Industrie et l'Agriculture, Belgique) for a fellowship (BR) and the FNRS (Fonds National de la Recherche Scientifique, Belgique) for their constant financial support (Mass Spectrometer and Polarimeter).

References and Notes

 (1) (a) Krief, A.; Barbeaux, P. J. Chem. Soc. Chem. Commun. 1987, 16, 1214-1216; (b) Krief, A.; Kenda, B.; Remacle, B. Tetrahedron 1996, 52, 7435-7463; (c) Krief, A.; Kenda, B.; Barbeaux, P.; Guittet, E. Tetrahedron 1994, 50, 7177-7192.

- (2) Comparatively the cyclization of 2a in ether is very slow at -78 °C. The presence of the phenyl group on the C,C double bond enhances dramatically the rate of the reaction in that solvent.
- (3) For related reactions producing benzyllithiums after carbocyclization (a) Wei, X.; Taylor, R.J.K. *Tetrahedron Lett.* **1997**, *38*, 6467; (b) Woltering, M.J.; Frölich, R.; Hoppe, D. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1764; (c) Tomooka, K.; Komine, N.; Sasaki, T.; Shimizu, H.; Nakai, T. *Tetrahedron Lett.* **1998**, *39*, 9715 (d) Bailey, W.F.; Gavaskar, K.V. *Tetrahedron* **1994**, *50*, 5957.
- (4) These reactions have been carried out with (a) 1.6 N n-BuLi in hexanes; (b) 1.3 N s-BuLi in cyclohexane or (c) 1.7 N t-BuLi in pentane all from the Aldrich Company.
- (5) For example when the reaction is carried out with *s*-BuLi in ether at -45 °C on a 50/50 or a 10/90 (Table, entry d) ratio of Z-1d/E-1d we obtained a 88/12 or a 90/10 ratio of 4'd/4''d. For a related result see : Hoffmann, R.W.; Koberstein, R.; Remacle, B.; Krief, A. *Chem. Commun.* 1997, 2189-2190.
- (6) **3"d** is usually produced when the carbocyclization is performed in THF. Using the strategy disclosed in this section we have been able to generate instead **3'd** in the same solvent.
- (8) (a) Bailey, W. F.; Carson, M. W. J. Org. Chem. 1998, 63, 361;
 (b) Coldham, I.; Hufton, R. Tetrahedron. 1996, 52, 12541.

Article Identifier:

1437-2096,E;1999,0,07,1142,1144,ftx,en;G09999ST.pdf