Tetrahedron Letters,Vol.26,No.4,pp 411-414,1985
Printed in Great Britain

0040-4039/85 $3.00 + .00

COMPLETELY STEREOSELECTIVE SYNTHESIS OF ALL FOUR STEREOISOMERIC 1-CARBAMOYLOXY-1,3-ALKADIENES VIA ANTI-DIASTEREOSELECTIVE HOMOALDOL REACTION FROM ALDEHYDES AND A SINGLE CARBON-THREE-UNIT

Ede van Hülsen and Dieter Hoppe*
Institute of Organic Chemistry, University of Göttingen, Tammannstraße 2, D-3400 Göttingen, FRG

Summary: *Lithiation of both (Z)- and (E)-3-trimethylsilyl-2-propenyl N,N-diisopropyl carbamate* **2** *affords the (2E)-lithium compound* **3**. *Aluminium- or titanium-mediated addition to aldehydes* **4** *gives (1E)-(3R*4S*)-enol carbamates* **7**. *A stereospecific Peterson elimination (borontrifluoride- or base-mediated) introduces the second double bond either with (3E)- or with (3Z)-configuration. So just by reagent selection for each of the two steps, (1E,3E)-, (1E,3Z)-, (1Z,3E)-, or (1Z,3Z)-dienes* **8** *-* **11**, *respectively, are prepared with stereoselectivities up to > 99.7 %.*

1-Oxy-1,3-alkadienes are of considerable preparative value in cycloaddition reactions[1]. Despite that, the access to configuratively pure members is rather limited[1,2]. We report now on a set of simple and efficient methods for the synthesis of all possible geometric isomers of 1,3-alkadienyl N,N-diisopropyl carbamates **8** - **11** from a given aldehyde **4**. The three-carbon extension is based on our versions of anti-diastereoselective homoaldol reaction[3], utilizing metal derivatives of the 3-trimethylsilyl-2-propenyl carbamates **2**, followed by stereospecific silanol eliminations[4,5].

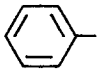
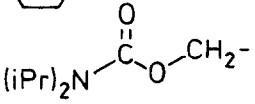
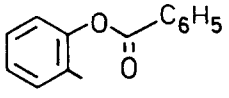
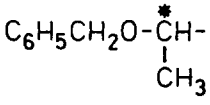
(E)-**2** is prepared[6] from (E)-trimethylsilyl-2-propenol[7] and diisopropylcarbamoyl chloride; (Z)-**2** is obtained from the propargylic ester[8] **1a** by lithiation and silylation via alkyne **1c** (yield 90 %) and subsequent nickel-catalyzed cis-hydrogenation by the method of C. A. Brown[9], yield 68 %. The lithiation (n-butyllithium in hexane, TMEDA, in ether, 1 hour at -78 °C) of both (E)- or (Z)-**2** forms the (2E)-anion **3**, which was trapped by trimethylsilyl chloride to afford the (E)-olefin **12**. Starting from (Z)-**2**, the topomerization of the double bond[10] is already complete after 5 min. at -78 °C, hence identical results are observed no matter if (E)- or (Z)-**2** or configuratively inhomogeneous starting material is used.

After exchange of lithium in (2E)-**3** with diisobutylaluminium methanesulfonate[11,12] (**5**, method A) or tris(dimethylamino)titanium chloride[13,14] (**6**, method B), the addition of an aldehyde **4** proceeds with high anti-diastereoselectivity[12,13] affording diastereomerically pure[15] (1E)- or (1Z)-(3R*, 4S*)-enolcarbamates[16] **7**, respectively, which are separated from side products by flash chromatography or recrystallization from pentane (see scheme and table). By stirring (E)- or (Z)-**7** with excess of borontrifluoride etherate in dichloromethane (method C) at -78 °C, a (3E)-double bond is established, yielding pure (1E,3E)- or (1Z,3E)-dienes **8** or **10**, whereas treatment of **7** with sodium hydride (in ether/THF, 0 °C; method D) gives rise to a (3Z)-double bond in (1E,3Z)- or (1Z,3Z)-dienes[17] **9** or **11** (see scheme and table). The diastereomeric purities of dienes **8a**, **8b**, **9a**, **10b**, **11a**, and **11b**, which are sufficiently volatile for capillary gaschromatographic analysis, were found to be > 99.7 %, here the limit of detection is < 0.1 % for each isomer.

Altogether, the method provides a highly selective access to all the diastereomeric alkadienes **8 - 11**, starting from a stereochemically inhomogenous precursor, since a stereoconvergent reaction step is placed before two stereodivergent steps.

In preliminary experiments, dienes **8** proved their suitability for Lewis-acid catalyzed Diels-Alder reactions. For instance, **8a** and acrolein afforded (BF_3-etherate, dichloromethane, 8 h at -23 °C) the cyclohexene **13** as a single (racemic) diastereomer [18] with 82 % yield.

Table: Yields (%) of enol carbamates **7** and dienes **8, 9, 10, 11** [a].

4, 7-11	R	(E)-7 [b] method A	(Z)-7 [b] method B	8 [c] method C	9 [c] method D	10 [d] method C	11 [d] method D
a	H_3C-	75	82	98 (>99.7) [e]	93 (>99.7) [e]	91 (99.2) [e]	98 (>99.7) [e]
b	H_3C, H_3C>CH-	76	85	93 (>99.7) [e,f]	92 (97.0) [g]	95 (>99.7) [e]	96 (>99.7) [e]
c		80	--	80 (>95) [h]	98 (>95) [h]	--	--
d		71	--	--	93 (>95) [h]	--	--
e		75	--	73 (>95) [h]	--	--	--
f		79 [i]	--	--	94 (>95) [h]	--	--

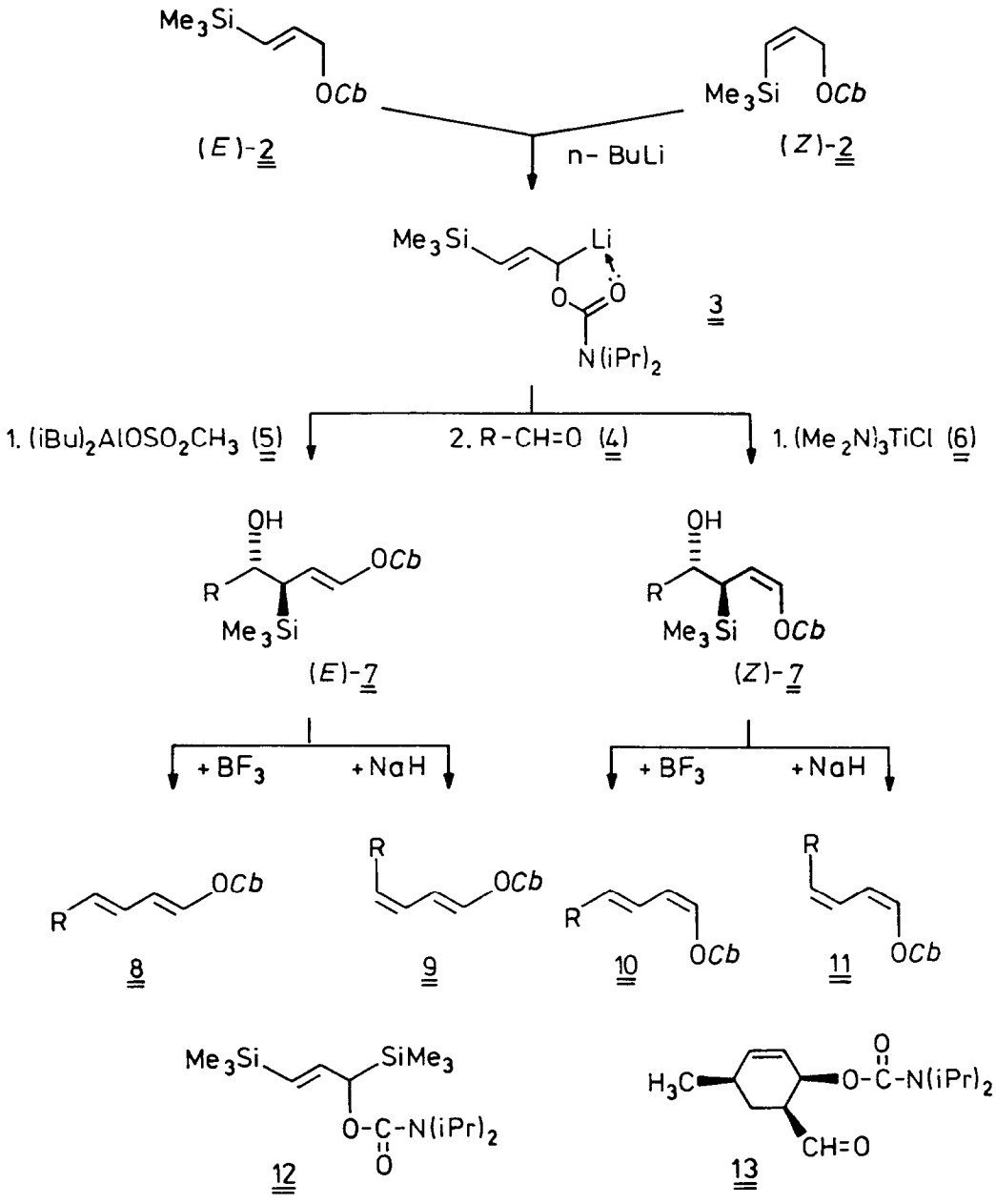
[a] The purity is listed in parentheses. - [b] Yield after chromatographic purification. No isomers are detected in ^{13}C-nmr spectra. - [c] With (E)-**7**. - [d] With (Z)-**7**. - [e] Determined by capillary gaschromatography on Carbowax 57 CB. - [f] The equal result was obtained with crude (E)-**7b**. - [g] Contains 3.0 % of **8b** which origins from 3 % of (E)-syn-**7b**, present in the batch used for this experiment (^{13}C-nmr, tlc). - [h] No isomers are detected in ^{13}C-nmr. - [i] Diastereomers.

General procedures; (E)-**3**: To 5.0 mmol (E)- or (Z)-**2** and 5.0 mmol TMEDA in 15 ml ether at -78 °C 5.5 mmol n-BuLi in hexane is added slowly and the mixture stirred for 1 hour.
Method A; (E)-**7**: 5.5 mmol **5** in tert.-butyl methyl ether (0.5 molar, prepared from DIBALH in hexane [11]) is added to the solution of (E)-**3**, followed by 5.0 mmol of aldehyde **4** at -78 °C. The mixture is stirred for 1 h and worked-up with aqueous K-Na-tartrate solution.
Method B; (Z)-**7**: 5.5 mmol **6** in hexane [14] is added to the solution of (E)-**3** at -78 °C, followed by **4** after 1 h at -78 °C. Stirring is continued for 4 h and the reaction mixture worked-up as usual with aqueous 1 N H_2SO_4.
Method C; **8** or **10**: A 0.3 molar solution of (E)-**7** or (Z)-**7** in dichloromethane is stirred with 2.5 equiv. of BF_3-etherate at -78 °C for 15 h and worked-up with aqueous $NaHCO_3$-solution.
Method D; **9** or **11**: A 0.3 molar solution of (E)-**7** or (Z)-**7** in ether/THF (1 : 1) is stirred with 2.5 equiv. of NaH for 3 h at 0 °C followed by cautious aqueous work-up.

$R\text{-}C{\equiv}C\text{-}CH_2\text{-}OCb$ $\quad Cb = C(=O)\text{-}N(iPr)_2$

1a R = H
b R = Li
c R = $SiMe_3$

Scheme 1



Acknowledgements: Financial support of this work by Deutsche Forschungsgemeinschaft and Fonds der Chemischen Industrie is gratefully acknowledged.

1) Reviews : M. Petrzilka, J. I. Grayson, Synthesis **1981**, 753; S. Danishefsky, Acc. Chem. Res. **14**, 400 (1982).

2) For more recent work and references see: A. K. Forrest, R. R. Schmidt, Tetrahedron Lett. **25**, 1769 (1984); see also ref. 18.

3) Review: D. Hoppe, Angew. Chem. **96**, issue 12 (1984), Angew. Chem., Int. Ed. Engl. **23**, issue 12 (1984).

4) Review: E. W. Colvin, Silicon in Organic Synthesis, Butterworth, London 1981, p. 141.

5) Synthesis of 1,3-alkadienes by similar strategies, which control the configuration of only one double bond, see: D. J. S. Tsai, D. S. Matteson, Tetrahedron Lett. **22**, 2751 (1981); F. Sato, Y. Suzuki, M. Sato, ibid., **23**, 4589 (1982); M. T. Reetz, B. Wenderoth, ibid. **23**, 5259 (1982); Y. Ikeda, K. Furuta, N. Meguriya, N. Ikeda, H. Yamamoto, J. Am. Chem. Soc. **104**, 7663 (1982). - Synthesis of (1E, 3 Z)- or (1E, 3E)-1-(trimethylsilyl)-1,3-alkadienes, see: T.-H. Chan, J.-S. Li, J. Chem. Soc., Chem. Commun. **1982**, 969; F. Sato, H. Uchiyama, K. Iida, Y. Kobayashi, M. Sato, ibid. **1983**, 921.

6) a) D. Hoppe, R. Hanko, A. Brönneke, F. Lichtenberg, Angew. Chem. **93** (1981) 1106; Angew. Chem., Int. Ed. Engl. **20** (1981) 1024; b) D. Hoppe, R. Hanko, A. Brönneke, F. Lichtenberg, E. van Hülsen, Chem. Ber. **118**, in press (1985).

7) S. E. Denmark, T. K. Jones, J. Org. Chem. **47**, 4595 (1982), and references.

8) D. Hoppe , C. Riemenschneider, Angew. Chem. **95**, 64 (1983); Angew. Chem., Int. Ed. Engl. **22**, 54 (1983).

9) C. A. Brown, V. K. Ahuja, J. Chem. Soc., Chem. Commun. **1973**, 553

10) In contrast, the appropriate 2-butenyl derivatives are configuratively stable at these conditions, see ref. 6b, 11.

11) D. Hoppe, F. Lichtenberg , Angew. Chem. **96**, 241 (1984); Angew. Chem., Int. Ed. Engl. **23**, 239 (1984).

12) D. Hoppe, F. Lichtenberg, Angew. Chem. **94**, 378 (1982); Angew. Chem. Int., Ed. Engl. **21**, 372 (1982); Angew. Chem. Suppl. **1982**, 961 - 972.

13) R. Hanko, D. Hoppe, Angew. Chem. **94**, 378 (1982); Angew. Chem., Int. Ed. Engl. **21**, 372 (1982); D. Hoppe, A. Brönneke, Tetrahedron Lett. **24**, 1687 (1982).

14) Reviews: M. T. Reetz, Top. Curr. Chem. **106**, 1 (1982); B. Weidmann, D. Seebach, Angew. Chem. **95**, 12 (1983); Angew. Chem. Int., Ed. Engl. **22**, 31 (1983); D. Seebach, B. Weidmann, L. Widler in (R. Scheffold) Modern Synthetic Methods **1983**, P. 217.

15) Diastereomers could not be detected by ^{1}H- and ^{13}C-nmr or by tlc of the crude reaction mixture. Crude (E)-**7b** and (Z)-**7a** gave dienes **8b** and **10a** of > 99 % purity; which means that here the diastereoselectivities of homoaldol reaction are > 99 %. The easy separation of by-products from **7** by chromatography or crystallization avoids a purification on the stage of **8 - 11**.

16) ^{1}H-nmr ($CDCl_3$, 80 MHz,δ);(E)-**7a**: 7.00 (d, $J_{1,2}$ = 12 Hz, H-1). 1.42 (dd, $J_{2,3}$ = 12 Hz; $J_{3,4}$ = 6 Hz, H-3); (Z)-**7a**: 7.08 (d, $J_{1,2}$ = 5.6 Hz, H-1), 2.05 (dd, $J_{2,3}$ = 12 Hz, $J_{3,4}$ = 5.6 H, H-3).

17) ^{1}H-nmr ($CDCl_3$), 80 MHz, δ); **9a**: 7.30 (d, $J_{1,2}$ = 11 Hz, H-1), 6.18 (dd, $J_{2,3}$ = 11 Hz, H-2), 5.90 (dd, $J_{3,4}$ = 12 Hz, H-3), 5.38 (dq, $J_{4,5}$ = 6.8 Hz, H-4). **10a**: 6.87 (d, $J_{1,2}$ = 6.6 Hz, H-1), 5.30 (dd, $J_{2,3}$ = 11 Hz, H-2), 6.31 (dd, $J_{3,4}$ = 15.6 Hz, H-3), 5.67 (dq, $J_{4,5}$ = 6.8 Hz, H-4). **11a**: 7.02 (d, $J_{1,2}$ = 6.4 Hz, H-1), 5.55 (dd, $J_{2,3}$ = 11 Hz, H-2), 6.29 (dd, $J_{3,4}$ = 11 Hz, H-3), 5.45 (dq, $J_{4,5}$ = 6.8 Hz, H-4). - **8a** (in C_6D_6, 200 MHz): 7.73 (d, $J_{1,2}$ = 12.4 Hz, H-1), 6.04 (dd, $J_{2,3}$ = 10.4 Hz, H-2), 5.82 (ddq, $J_{3,4}$ = 15.6 Hz, $J_{3,5}$ = 1.0 Hz, H-3), 5.43 (dq, $J_{4,5}$ = 7.2 Hz, H-4).

18) The ^{1}H-nmr data are in good agreement with these of a similar compound (OAc for OCb, Et for Me in **13**); see: B. M. Trost, S. A. Godleski, J. P. Genêt, J. Am. Chem. Soc. **100**, 3930 (1978).

(Received in Germany 7 November 1984)