Table II. Photosensitized Transacetalization[a]

substrate	nucleophile	substrate conversion, %[b]	acetal product % yield[b,c] (cis:trans)[b]
3	n-$C_8H_{17}OH$	78	88
3	n-$C_8H_{17}OSi(CH_3)_3$	75	55
3	$C_6H_5CH_2OH$	80	84
3	c-$C_6H_{11}OH$	66	81
3	n-$C_4H_9(CH_3)_2COH$	53	44[d]
3	C_6H_5OH	77	16[d]
cis-**4**	n-$C_8H_{17}OH$	100	86 (11:89)[e]
trans-**4**	n-$C_8H_{17}OH$	96	86 (11:89)
4 (cis:trans = 52:48)	n-$C_8H_{17}OH$	85	87 (11:89)
4 (cis:trans = 52:48)	c-$C_6H_{11}OH$	63	79 (15:85)[e]
4 (cis:trans = 52:48)	n-$C_4H_9(CH_3)_2COH$	65	45[d] (14:86)[f]

[a] Reaction was conducted by irradiation of a mixture of the substrate, nucleophile, phenanthrene (10%), and *p*-dicyanobenzene (10%) in acetonitrile with a 200-W high-pressure Hg arc at 20 °C for 10 h. [b] Determined by GLC analysis. [c] Based on conversion. [d] The major byproduct was a 3,4-dihydro-2*H*-pyran. [e] The thermodynamic ratio is 40:60. [f] The thermodynamic ratio is 36:64.

ion **6**. It should be added that the sensitized photolysis of pure *cis*- or *trans*-**4** in the absence of any nucleophiles did not cause significant cis–trans isomerization; at low conversion,[9] decomposition to the dihydropyran and phenolic products was the major reaction course. This implies that the intermediary oxocarbenium ion and aryl oxide ion are cage separated and that possible recombination, giving back the starting material, is negligible under the reaction conditions.

The present phototransacetalization is achievable under nearly neutral conditions. Some preliminary experiments suggested its synthetic potentiality in glycosidation. Photoirradiation of the protected 2-deoxyglucoside **7** (α:β = 30:70) and 1-octanol under the standard conditions (10% phenanthrene/DCNB in acetonitrile, 20 °C, 15 h) gave the octyl 2-deoxyglucoside **8** in 89% yield (80% conversion, α:β = 55:45). In addition, exposure of **9** to the photosensitized conditions caused intramolecular acetalization (20 °C, 30 h) to give the 1,6-anhydro sugar **10** in 96% yield (38% conversion).

Most nucleophilic substitutions occur by two-electron-exchange mechanisms in an S_N1 or S_N2 manner. Here we disclosed a clear-cut example of the $S_{ON}1$ process[10] proceeding via one-electron-exchange mechanism.[11]

Acknowledgment. We thank Professors J. P. Dinnocenzo, N. Kornblum, T. Matsuura, J. Tanaka, and D. G. Whitten and Dr. K. Takagi for valuable discussions and suggestions on the reaction mechanism and technical problems.

Registry No. 2 (R = $(CH_2)_8$-$OSi(CH_3)_3$), 70690-19-6; **2** (R = $C_6H_5CH_2$), 1927-62-4; **2** (R = c-C_6H_{11}), 709-83-1; **2** (R = $C_4H_9(CH_3)_2C$), 94800-78-9; **2** (R = C_6H_5), 4203-50-3; **3** (AR = 2,4,6-$(CH_3)_3C_6H_2$), 94800-75-6; *cis*-**4**, 94800-76-7; *trans*-**4**, 94800-77-8; *cis*-**5** (R = C_8H_{17}), 94800-79-0; *trans*-**5** (R = C_8H_{17}), 94800-80-3; *cis*-**5** (R = C_6H_{11}), 94800-81-4; *trans*-**5** (R = C_6H_{11}), 94800-82-5; *cis*-**5** (R = $C_4H_9(CH_3)_2C$), 94800-83-6; *trans*-**5** (R = $C_4H_9(CH_3)_2C$), 94800-84-7; **7** (α-isomer), 94800-85-8; **7** (β-isomer), 94800-86-9; **8** (α-isomer), 94800-87-0; **8** (β-isomer), 94800-88-1; **9**, 94800-89-2; **10**, 2951-86-2; 1-octanol, 111-87-5; 3,4-dihydro-2*H*-pyran, 110-87-2; $C_8H_{17}OSi(CH_3)_3$, 14246-16-3; $C_6H_5CH_2OH$, 100-51-6; c-$C_6H_{11}OH$, 108-93-0; $C_4H_9(CH_3)_2COH$, 625-23-0; C_6H_5OH, 108-95-2.

(9) At high conversion, some cis to trans (but not trans to cis) isomerization was observed. Addition of 2,4,6-trimethylphenol to the reaction system, of course, caused the isomerization.

(10) Possible chain reactions: Alder, R. W. *J. Chem. Soc., Chem. Commun.* **1980**, 1184–1186.

(11) For $S_{ON}2$ reaction (chain mechanism), see: Eberson, L.; Jönsson, L. *J. Chem. Soc., Chem. Commun.* **1980**, 1187–1188; **1981**, 133–134. $S_{RN}1$ reactions (chain mechanism) are well-known. For example: Kornblum, N.; Michel, R. E.; Kerber, R. C. *J. Am. Chem. Soc.* **1966**, *88*, 5660–5662. Russell, G. A.; Danen, W. C. *Ibid.* **1966**, *88*, 5663–5665. Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413–420.

Ester Homologation via α-Bromo α-Keto Dianion Rearrangement

Conrad J. Kowalski,*[1a] M. Serajul Haque,[1a] and Kevin W. Fields[1b]

Synthetic Chemistry Department
Smith Kline and French Laboratories
P.O. Box 7929, Philadelphia, Pennsylvania 19101
Department of Chemistry, University of Notre Dame
Notre Dame, Indiana 46556

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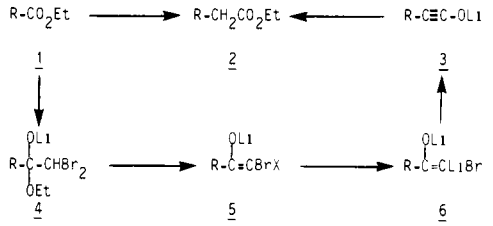
Herein we report on the mechanism, stereochemistry, and scope of a new procedure for the homologation of esters (i.e., **1** → **2**) and its application to the synthesis of the antifungal antibiotic oudemansin (**32**). This method is based upon our previously reported rearrangement reaction[2] of α-halo α-keto dianions **6** to alkynolate anions **3**, which afford esters **2** upon quenching into



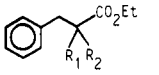
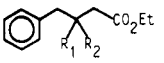
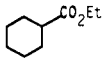
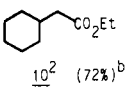
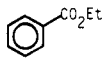
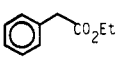
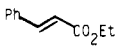
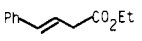
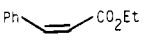
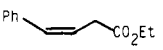
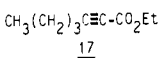
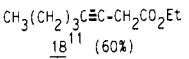
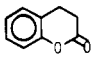
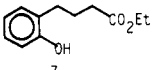
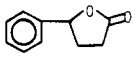
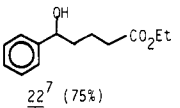
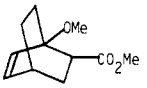
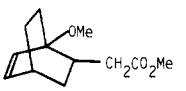
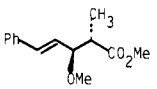
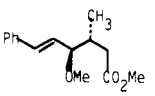
acidic alcohol solutions. In the present application of this rearrangment, esters **1** are treated with dibromomethyllithium at −90 °C by using a modification[3] of the procedure of Normant.[4] Depending upon the nature of the ester R group, this affords mixtures of tetrahedral intermediate **4**, dibromo ketone enolate **5a** (X = Br), and/or monobromo ketone enolate **5b** (X = H). Subsequent addition of n-butyllithium at −90 °C results in rapid metal–halogen exchange with any **4** present to afford **5b** (X = H) and with any **5a** (X = Br) present to afford **3** (from rearrangement of **6**; i.e., **5a** → **6** → **3**). Enolates **5b** (X = H) are unreactive in these mixtures at low temperatures, but undergo deprotonation near 0 °C by lithium tetramethylpiperidide present; thus, in order to ensure complete conversion of any **5b** (X = H) present to **3** (i.e., **5b** → **6** → **3**), these solutions are warmed to room temperature. In this manner all the intermediates (**4**, **5a**, and **5b**) obtained from ester **1** can be converted to alkynolate anion **3** via rearrangement of **6**. Formation of ester **2** on quenching results overall in the net homologation of starting ester **1**.

Applications of this chemistry shown in Table I demonstrate its utility for esters **1** bearing R groups that are primary, secondary, tertiary, aryl, alkenyl, and alkynyl and for some lactones as well. In a typical procedure, performed under a N_2 atmosphere, 4.4 mmol of *n*-butyllithium solution in hexane was added dropwise

(1) (a) Smith Kline and French. (b) The Upjohn Co., Kalamazoo, MI.
(2) Kowalski, C. J.; Fields, K. W. *J. Am. Chem. Soc.* **1982**, *104*, 321.
(3) It is important that lithium tetramethylpiperidide be used to deprotonate the methylene bromide in this step, to avoid formation of undesired dialkylamide byproducts (corresponding to esters **2**) in the final quench.
(4) Villieras, J.; Bacquet, C.; Normant, J.-F. *Bull. Soc. Chim. Fr.* **1975**, 1797.
(5) Sekine, M.; Nakajima, M.; Kum, A.; Hashizume, A.; Hata, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 224.
(6) Terashima, S.; Tseng, C. C.; Koga, K. *Chem. Pharm. Bull.* **1979**, *27*, 747.
(7) All new compounds afforded proper combustion analysis as well as IR, NMR, and mass spectra.
(8) Gerkin, R. M.; Rickborn, B. *J. Am. Chem. Soc.* **1967**, *89*, 5850.
(9) Prepared via hydrogenation of the corresponding alkyne over Lindlar catalyst; for a similar prep, see: Savoia, D.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1981**, *46*, 5344.
(10) Uijttewaal, A. P.; jonkers, F. L.; van der Gen, A. *J. Org. Chem.* **1979**, *44*, 3157.
(11) Hooz, J.; Layton, R. B. *Can. J. Chem.* **1972**, *50*, 105.
(12) From chromatographic separation of commercially available material (Aldrich).

0002-7863/85/1507-1429$01.50/0

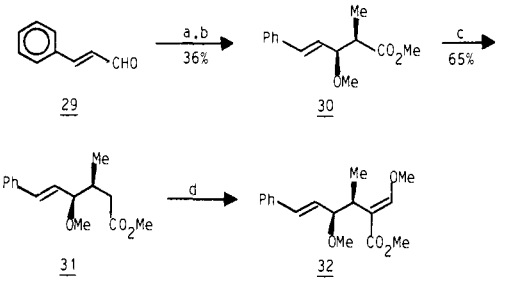
Table I

starting ester	product (yield)[a]
 7a: R_1=H, R_2=H; b:[6] R_1=H, R_2=Me; c:[7] R_1=Me, R_2=Me	 8a:[5] (74%); b:[5] (74%)[b]; c:[7] (72%)
 9	 10[2] (72%)[b]
 11	 12 (65%)
 13	 14[8] (53%)[c]
 15[9]	 16[10] (55%)[c]
 17	 18[11] (60%)
 19	 20[7] (72%)
 21	 22[7] (75%)
 23 [endo][12]; 25 [exo][12]	 24 [endo][7] (60%)[c]; 26 [exo][7] (57%)[c]
 27[7]	 28[7] (60%)[c]

[a] Isolated, purified material; from standard procedure (2.2 equiv of $LiCHBr_2$, then 5 equiv of *n*-BuLi) unless noted. [b] 2.2 equiv of $LiCHBr_2$, then 1 equiv of tetramethylpiperidine, then 6 equiv of *n*-BuLi. [c] 3.3 equiv of $LiCHBr_2$, then 1 equiv of tetramethylpiperidine, then 8 equiv of *n*-BuLi.

to a stirred, 0 °C solution of 4.8 mmol of 2,2,6,6-tetramethylpiperidine in 6 mL of THF. This mixture was added dropwise to a stirred solution of 4.4 mmol of dibromomethane in 6 mL of THF, cooled with a −90 °C bath (dry ice/diethyl ether). After 5 min, a solution of 2.0 mmol of ethyl dihydrocinnamate (**7a**) in 5 mL of THF was added dropwise, and 10 min later a solution of 10 mmol of *n*-butyllithium in hexane was added dropwise. The −90 °C cooling bath was then replaced with a 30 °C water bath, and after it was stired for 15 min the reaction mixture was added via cannula to a rapidly stirred, ice-cooled solution of acidic ethanol (prepared from 5 mL of acetyl chloride in 25 mL of absolute ethanol). The mixture was diluted with 200 mL of ether, washed with 10% sulfuric acid, 5% aqueous sodium bicarbonate, and saturated brine, and purified by preparative silica gel TLC to afford homologated ester **8a** in 74% yield. In some cases, a higher ratio of reagents to ester was necessary to effect complete addition of dibromomethyllithium to ester or complete conversion of enolate **5b** to alkynolate **3**.

Scheme I[a]



[a] (a) $CH_3CHBrCO_2Me$, Zn, PhH, Δ. (b) KH, Me_2SO_4, THF, −78 °C → room temperature. (c) $LiCHBr_2$, −90 °C; BuLi, −90 °C → room temperature; MeOH, HCl. (d) Reference 13.

Of particular interest in Table I are the homologations of compounds **13**, **15**, **23**, and **25**, each of which produced only a single ester product; in every case, rearrangement occurred with complete retention of stereochemistry, and no trace of isomeric products was detected. Such stereospecificity of the homologation reaction made possible its use in a formal synthesis of the antibiotic oudemansin (**32**), patterned after the original efforts of Nakata and Oishi.[13] In their work, *d,l* ester **30** (prepared in 35% yield from **29** via a four-step sequence) was homologated to ester **31** using the classical Arndt–Eistert[14] aproach, and **31** was converted to *d,l*-oudemansin (**32**) (Scheme I) in two more steps. The homologation entailed hydrolysis, acid chloride formation, diazomethane addition, and silver-catalyzed Wolff rearrangement to afford ester **31** in 52% yield from **30** after four steps.

Our efforts utilized the Reformatsky reaction of methyl 2-bromopropionate with cinnamaldehyde (**29**) as in the previous synthesis[13] but followed this by direct methylation (KH, dimethyl sulfate, THF) to afford (after silica gel chromatography) the desired ester **30** and its diastereomer **27** in 36% and 37% yield, respectively. Application of our homologation procedure (incorporating an acidic methanol quench) to ester **30** afforded ester **31**[13] in 65% yield, while application to the diastereomer **27** afforded ester **28**[7] in 60% yield. In each case only a single diastereomeric product was obtained, with none of the other observed. This three-step synthesis of ester **31** from cinnamaldehyde (23% overall) compares favorably with the original eight-step route (18%) and constitutes a formal synthesis of *d,l*-oudemansin. More importantly, successful homologation of this sensitive molecule containing an allylic methoxy group β to a stereochemically defined ester moiety nicely illustrates the potential of this new methodology for natural product synthesis.

Acknowledgment. Early phases of this work were supported by the National Cancer Institute Grant 27157 and National Science Foundation Grant CHE-8111128; most was supported via a postdoctoral fellowship to M. S. Haque at SK&F.

Registry No. **7a**, 2021-28-5; **7b**, 34666-01-8; **7c**, 94800-92-7; **8a**, 10031-93-3; **8b**, 72277-22-6; **8c**, 94800-93-8; **9**, 3289-28-9; **10**, 5452-75-5; **11**, 93-89-0; **12**, 101-97-3; **13**, 4192-77-2; **14**, 1205-84-1; **15**, 4610-69-9; **16**, 78000-63-2; **17**, 16930-95-3; **18**, 37174-93-9; **19**, 119-84-6; **20**, 20921-17-9; **21**, 1008-76-0; **22**, 94800-94-9; **23**, 25582-95-0; **24**, 94800-95-0; **25**, 25516-76-1; **26**, 94842-46-3; **27**, 94842-47-4; **28**, 94842-48-5; (±)-**30**, 82414-47-9; (±)-**31**, 88155-83-3; (±)-**32**, 82444-24-4; (*E*)-PhCH=CHCHO, 14371-10-9; (±)-$CH_3CHBrCo_2Me$, 57885-43-5; dibromomethane, 74-95-3; dibromomethyllithium, 37555-63-8.

Supplementary Material Available: IR, NMR, mass spectra and combustion analyses for **7c**, **8c**, **20**, **22**, **26–28**, **30**, and **31** (2 pages). Ordering information is given on any current masthead page.

(13) Nakata, T.; Kuwabara, T.; Tani, Y.; Oishi, T. *Tetrahedron Lett.* **1982**, *23*, 1015.
(14) Backmann, W. E.; Struve, W. S. *Org. React.* (*N.Y.*) **1942**, *1*, 38.