Table II. Photosensitized Transacetalization^a

substrate	nucleophile	substrate conver- sion, % ^b	acetal product % yield ^{b,c} (cis:trans) ^b
3	<i>n</i> -C ₈ H ₁₇ OH	78	88
3	$n-C_8H_{17}OSi(CH_3)_3$	75	55
3	C ₆ H ₅ CH ₂ OH	80	84
3	c-C ₆ H ₁₁ OH	66	81
3	$n-C_4H_9(CH_3)_2COH$	53	44 ^d
3	C ₆ H ₅ OH	77	16 ^d
cis-4	<i>n</i> -C ₈ H ₁₇ OH	100	86 (11:89) ^e
trans-4	<i>n</i> -C ₈ H ₁₇ OH	96	86 (11:89)
4 (cis:trans = 52:48)	<i>n</i> -C ₈ H ₁₇ OH	85	87 (11:89)
4 (cis:trans = 52:48)	c-C ₆ H ₁₁ OH	63	79 (15:85) ^e
4 (cis:trans = 52:48)	<i>n</i> -C ₄ H ₉ (CH ₃) ₂ COH	65	$45^d (14:86)^f$

^aReaction 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. ^cBased on conversion. ^d The major byproduct was a 3,4-dihydro-2*H*-pyran. ^eThe thermodynamic ratio is 40:60. ^fThe 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 ($\alpha:\beta = 30:70$) 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, $\alpha:\beta = 55:45$). 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 $S_{\rm N}1$ or $S_{\rm N}2$ manner. Here we disclosed a clear-cut example of the $S_{\rm ON}1$ process^{10} proceeding via one-electron-exchange mechanism. 11

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Registry No. 2 (R = (CH₂)₈-OSi(CH₃)₃), 70690-19-6; **2** (R = C₆H₅CH₂), 1927-62-4; **2** (R = c-C₆H₁₁), 709-83-1; **2** (R = C₄H₉-(CH₃)₂C), 94800-78-9; **2** (R = C₆H₅), 4203-50-3; **3** (AR = 2,4,6-(CH₃)₃C₆H₂), 94800-75-6; *cis*-4, 94800-76-7; *trans*-4, 94800-77-8; *cis*-5 (R = C₈H₁₇), 94800-80-3; *cis*-5 (R = C₆H₁₁), 94800-81-4; *trans*-5 (R = C₆H₁₁), 94800-82-5; *cis*-5 (R = C₄H₉(CH₃)₂C), 94800-83-6; *trans*-5 (R = C₄H₉(CH₃)₂C), 94800-83-6; *trans*-5 (R = C₄H₉(CH₃)₂C), 94800-84-7; 7 (*α*-isomer), 94800-85-8; 7 (*β*-isomer), 94800-88-1; **9**, 94800-86-9; **8** (*α*-isomer), 94800-87-0; **8** (*β*-isomer), 94800-88-1; **9**, 94800-87-2; **1**, 2951-86-2; 1-octanol, 111-87-5; 3,4-dihydro-2*H*-pyran, 110-87-2; C₈H₁₇OSi(CH₃)₃, 14246-16-3; C₆H₅CH₂OH, 100-51-6; c-C₆H₁₁OH, 108-93-0; C₄H₉(CH₃)₂COH, 625-23-0; C₆H₅OH, 108-95-2.

Ester Homologation via α -Bromo α -Keto Dianion Rearrangement

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Herein we report on the mechanism, stereochemistry, and scope of a new procedure for the homologation of esters (i.e., $1 \rightarrow 2$) and its application to the synthesis of the antifungal antibiotic oudemansin (32). This method is based upon our previously reported rearrangement reaction² 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 modification³ 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., $5a \rightarrow 6 \rightarrow 3$). 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., $5b \rightarrow 6 \rightarrow 3$), 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

(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.
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Table I



^a Isolated, purified material; from standard procedure (2.2 equiv of LiCHBr₂, then 5 equiv of *n*-BuLi) unless noted. ^b 2.2 equiv of LiCHBr₂, then 1 equiv of tetramethylpiperidine, then 6 equiv of *n*-BuLi. ^c 3.3 equiv of LiCHBr₂, 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% vield. In some cases, a higher ratio of reagents to ester was necessary to effect complete addition Scheme I^a

31

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^a (a) CH₃CHBrCO₂Me, Zn, PhH, Δ . (b) KH, Me₂SO₄, THF, -78 °C \rightarrow room temperature. (c) LiCHBr₂, -90 °C; BuLi, -90 °C \rightarrow room temperature; MeOH, HCl. (d) Reference 13.

of dibromomethyllithium to ester or complete conversion of enolate **5b** to alkynolate **3**.

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-Eistert¹⁴ 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 2bromopropionate with cinnamaldehyde (29) as in the previous synthesis¹³ 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.

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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; (\pm) -30, 82414-47-9; (\pm) -31, 88155-83-3; (\pm) -32, 82444-24+4; (E)-PhCH==CHCHO, 14371-10-9; (\pm) -CH₃CHBrCo₂Me, 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.

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