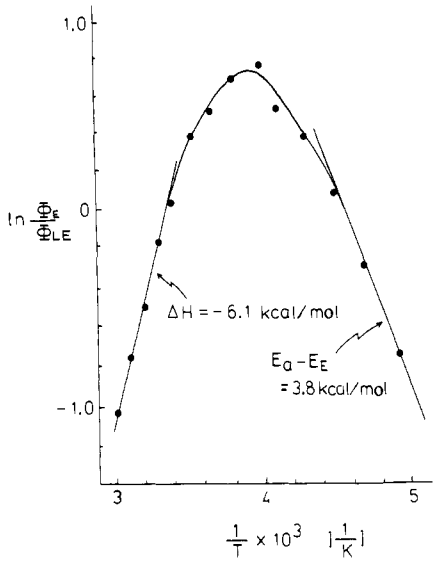
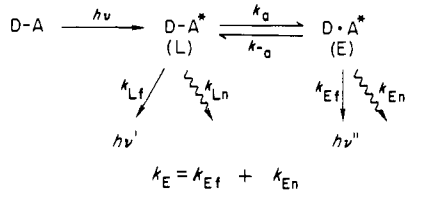


Figure 2. Effect of the temperature on the ratio of the quantum yields of fluorescence from the exciplex and locally excited states of the racemic isomer of **1**.

showed only the latter emission. The different emission character of the two isomers is consistent with the structural features of the stereoisomerism.[1] The exciplex fluorescence in the racemic compound indicates that when A* is formed by light absorption internal rotation takes place during the lifetime of A* to bring D to the proximity and generate D·A* complex. There is no such conformation accessible in the meso isomer. The processes are formulated as in Scheme II, where k_f and k_n are the radiative and nonradiative decay constants, respectively. In n-Bu_2O at 23 °C, the quantum yields of fluorescence of the locally excited naphthalene (Φ_L) and exciplex (Φ_E) were 0.068 and 0.070, respectively. The fluorescence quantum yield of the meso isomer was 0.19. Under photostationary conditions, $\Phi_E/\Phi_L = k_a k_{Ef}/k_{Lf}(k_{-a} + k_E)$. Therefore the temperature dependence of the ratio Φ_E/Φ_L is related to the activation energy ($E_a - E_E$) and enthalpy ($\Delta H°$) of formation of D·A*.[4] Such plots are given in Figure 2. In the high-temperature region, $k_E << k_{-a}$ and therefore $\ln(\Phi_E/\Phi_L) = -\Delta H/RT$. In the low-temperature region, $k_E >> k_{-a}$ and therefore $\ln(\Phi_E/\Phi_L) = -(E_a - E_E)/RT$. The E_a and $\Delta H°$ values in n-Bu_2O were obtained as 4.8 and -6.1 kcal/mol, respectively.[5]

In reference to Scheme II, the E_a value is associated with the height of the barrier over which the conformer with proximal D and A* is formed from the one with distal D and A* via torsional motions.[6] Whereas the naphtho group is in the electronic excited state, the gear framework of the molecule should not be very

Scheme II



different from that of the ground state. Therefore the E_a value of 4.8 kcal/mol is concluded to be a good measure of the barrier height to the gear-meshing process of **1**.[6]

Acknowledgment. We are grateful to Professor F. C. De Schryver of the Catholic University, Leuven, for helpful discussion.

Registry No. *dl*-**1**, 94800-91-6; *meso*-**1**, 94842-45-2.

(5) The E_E value was found independently by a transient experiment to be 0.98 kcal/mol (to be published).

(6) May we equate E_a to the activation energy to the geared rotation in **1**? The (dimethylamino)methyl group is considered to have additional modes of freedom, torsion around the CH_2–NMe_2 bond and nitrogen inversion, which might be attributed to the observed activation energy. According to DNMR experimental data, the barriers to these motions in appropriately substituted amines are in the range 6–8 kcal/mol: (a) Asahi, Y.; Numata, M.; Mizuta, E. *Chem. Pharm. Bull.* **1973**, *21*, 112. (b) Bushweller, C. H.; Anderson, W. G.; Stevenson, P. E.; Burkey, D. L.; O'Neil, J. W. *J. Am. Chem. Soc.* **1974**, *96*, 3892. (c) Sternhell, S. In "Dynamic Nuclear Magnetic Resonance Spectroscopy"; Jackson, L. M., Cotton, F. A., Eds.; Academic Press: New York, 1975; Chapter 6. The observed value is slightly too low to be assigned to such processes. In this connection, the obtained E_a of 4.8 kcal/mol is reasonably assigned to that required for torsion around the ether bond, namely, geared rotation. There may be intrinsic activation energy necessary for the formation of D·A* in which the amino group is thought to assume the planar configuration; a certain amount of energy of activation is needed for the configurational change. It is well established that D·A* is stabilized by solvation at the cost of a small amount of activation energy.[4] In other words, the E_a value may contain the barrier due to frictional forces with solvent molecules; See, for example: (a) Velsko, S. P.; Fleming, G. R. *J. Chem. Phys.* **1982**, *76*, 3553. (b) Velsko, S. P.; Fleming, G. R. *Chem. Phys.* **1982**, *65*, 59. If these activation energy values are not negligibly small, the observed value of 4.8 kcal/mol has to be taken as the upper limit of the unimolecular torsional barrier.

Novel Nucleophilic Substitution Reaction by Radical Cation Intermediates. Photosensitized Transacetalization via $S_{ON}1$ Mechanism

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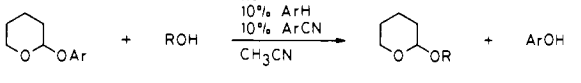
Generation of radical cations provides a new way to activate organic molecules.[1] In solution, radical cations can dissociate into the solvent-separated cations and radicals, thereby offering opportunities of a new type of metatheses (eq 1).[2] We disclose

$$\text{A–B} \xrightarrow{-e} \text{A–B}^{+}\cdot \rightarrow \text{A}^{+} + \cdot\text{B} \xrightarrow{e,\ \text{X–Y}} \text{A–X} + \text{B–Y} \quad (1)$$

here a newly designed substitution reaction involving a photostimulated one-electron-transfer process.[3]

What appeared to be crucial for the reaction of eq 1 to proceed smoothly were (1) relatively low oxidation potential of substrate A–B, (2) high stability of A^+ and B·, and (3) a suitable redox system allowing facile back electron transfer to convert B· to B^-. We found that transacetalization between aryl 2-tetrahydropyranyl ethers (**1**) and alcohols, giving **2** and phenols, was effected by the



1, Ar = aryl
3, Ar = 2,4,6-$(CH_3)_3C_6H_2$
2

photoexcitation technique using a binary sensitizing system consisting of a light-absorbing, condensed aromatic hydrocarbon and a non-light-absorbing cyano aromatic compound.[4] Table I lists

(1) A pertinent review on gas-phase reactions: Morton, T. H. *Tetrahedron* **1982**, *38*, 3195–3243.

(2) Arnold, D. R.; Maroulis, A. J. *J. Am. Chem. Soc.* **1976**, *98*, 5931–5937. Lin, C.; Singh, P.; Ullman, E. F. *Ibid.* **1976**, *98*, 6711–6713.

(3) Reviews on photostimulated one-electron-transfer reactions: Albini, A. *Synthesis* **1981**, 249–264. Mattes, S. L.; Farid, S. *Acc. Chem. Res.* **1982**, *15*, 80–86. Mattes, S. L.; Farid, S. In "Organic Photochemistry"; Padwa, A., Ed.; Marcel Dekker: New York and Basel, 1983; Vol. 6, pp 233–326.

(4) Pac, C.; Nakasone, A.; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 5806–5808. Majima, T.; Pac, C.; Nakasone, A.; Sakurai, H. *Ibid.* **1981**, *103*, 4499–4508. Majima, T.; Pac, C.; Sakurai, H. *Ibid.* **1980**, *102*, 5265–5273; *J. Chem. Soc., Perkin Trans. 1* **1980**, 2705–2708; *Chem. Lett.* **1979**, 1133–1136. Gotoh, T.; Kato, M.; Yamamoto, M.; Nishijima, Y. *J. Chem. Soc., Chem. Commun.* **1981**, 90–91. Tazuke, S., Kitamura, K. *Ibid.* **1977**, 515–516. Schaap, A. P.; Lopez, L.; Anderson, S. D.; Gagnon, S. D. *Tetrahedron Lett.* **1982**, *23*, 5493–5496. Schaap, A. P.; Lopez, L.; Gagnon, S. D. *J. Am. Chem. Soc.* **1983**, *105*, 663–664. Schaap, A. P.; Siddiqui, S.; Gagnon, S. D.; Lopez, L. *Ibid.* **1983**, *105*, 5149–5150.

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Table I. Photosensitized Transacetalization of 2-Tetrahydropyranyl 2,4,6-Trimethylphenyl Ether and 1-Octanol[a]

sensitizer system		substrate conversion, %[c]
hydrocarbon ($E_{ox}^{p/2}$, V)[b]	cyano aromatic ($-E_{red}^{p/2}$, V)[b]	
benzene (2.34)	*p*-dicyanobenzene (1.62)	14, 18[d]
triphenylene (1.74)	*p*-dicyanobenzene	76
phenanthrene (1.64)	*p*-dicyanobenzene	78
phenanthrene	1-cyanonaphthalene (1.58)	72
phenanthrene	9,10-dicyanoanthracene (0.86)	38
naphthalene (1.63)	*p*-dicyanobenzene	55
chrysene (1.48)	*p*-dicyanobenzene	72
anthracene (1.17)	*p*-dicyanobenzene	19

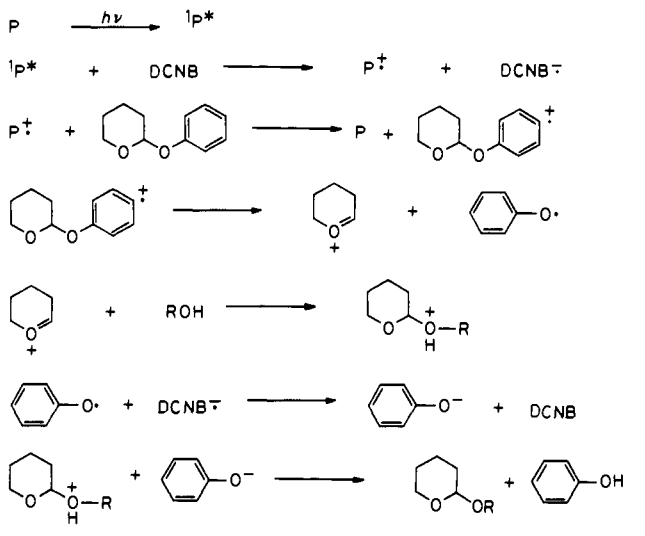
[a] External irradiation was carried out in an acetonitrile solution (with added molecular sieves, 4A) containing 8×10^{-2} M **3**, an aromatic hydrocarbon (8×10^{-3} M, 0.1 equiv), and a cyano aromatic (8×10^{-3} M, 0.1 equiv) placed in a Pyrex vessel with a 200-W high-pressure mercury lamp at 20 °C for 10 h. 1-Octyl 2-tetrahydropyranyl ether and 2,4,6-trimethylphenol were obtained in 75–100% and 100% yields (GLC assay), respectively, on the basis of the consumed starting material. The sensitizers were recovered in nearly quantitative yields. [b] Carbon electrode, sodium perchlorate (0.07 M) in acetonitrile, vs. Ag/AgCl. [c] Determined by GLC analysis. [d] Reaction in the absence of benzene.

some results of the transacetalization of the aryl 2-tetrahydropyranyl ether **3** with 1-octanol achieved by irradiation of a dry acetonitrile solution. Usually combination of a hydrocarbon with a high oxidation potential and a cyano aromatic with a high reduction potential afforded satisfactory results. A phenanthrene/*p*-dicyanobenzene (DCNB) or triphenylene/DCNB system is the typical example. The quantum yields measured for the formation of the acetal and 2,4,6-trimethylphenol (phenanthrene/DCNB cosensitizing system in acetonitrile, 366 nm, conversion <2%) were 0.020 and 0.023, respectively.

The photoinduced reaction of phenyl 2-tetrahydropyranyl ether (**1**, Ar = C_6H_5) and ROH is considered to occur by the mechanism outlined in Scheme I. Light absorption by phenanthrene produces its excited singlet state, which in turn is oxidized by ground-state DCNB, causing charge separation of the aromatic sensitizers. The hydrocarbon radical cation thus generated abstracts an electron from the phenoxy substrate to produce its radical cation, which collapses to the oxocarbenium ion and phenoxy radical. The oxocarbenium ion is then captured by an alcoholic nucleophile, whereas back electron transfer from $DCNB^{-\cdot}$ to phenoxy radical gives phenoxide ion and ground-state DCNB. Finally, proton reorganization affords the alkyl 2-tetrahydropyranyl ether **2** and phenol, establishing the catalytic cycle.

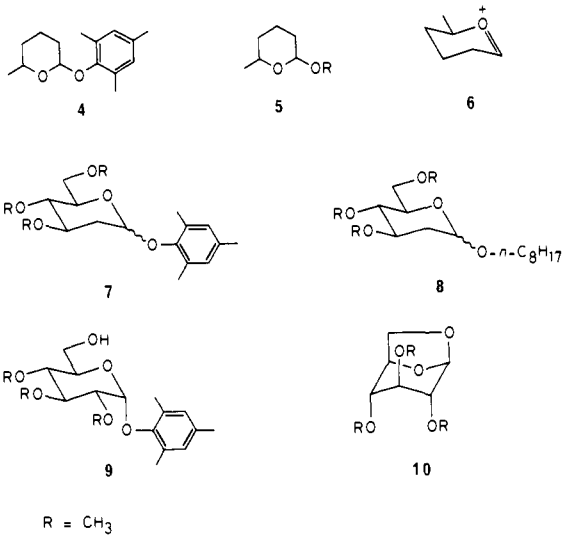
Operation of this mechanism was supported by various experimental observations. The hydrocarbon sensitizers with high oxidation potentials can generate the radical cations acting as powerful oxidizing agents. Radical anions of cyano aromatics with high reduction potentials reduce easily aryloxy radicals to give the aryl oxide ions. *p*-Dimethoxybenzene ($E_{ox}^{p/2}$ = 1.21 V vs. Ag/AgCl in CH_3CN) retarded the reaction by quenching the excited state of phenanthrene (proved by a fluorescence quenching experiment, $k_q = 5 \times 10^8$ M^{-1} s^{-1}) and by reducing the phenanthrene radical cation. Examination of the effect of the leaving groups on the photoinduced transacetalization using the phenanthrene/DCNB cosensitizing system revealed that the substrates should have lower oxidation potentials than phenanthrene ($E_{ox}^{p/2}$ = 1.64 V). Polyalkylated phenoxy groups thus generally served as a good leaving group. *p*-Nitrophenyl or 2,3,5,6-tetrafluorophenyl 2-tetrahydropyranyl ether ($E_{ox}^{p/2} > 2.0$ V) was almost inert to the reaction conditions. The *p*-methoxyphenyl derivative (**1**, Ar = *p*-$CH_3OC_6H_4$) having a low oxidation potential was unexpectedly unreactive. This is partly due to quenching of the excited state of phenanthrene, as has been observed with *p*-dimethoxybenzene. In addition, rapid back electron transfer from DCNB radical anion to the rather stable *p*-$CH_3OC_6H_4OTHP$ radical cation could also participate in the retardation of the substitution. As to nucleophiles, various alcohols afforded the corresponding alkyl 2-tetrahydropyranyl ethers.[5] When a sterically hindered

Scheme I



tertiary alcohol or weakly nucleophilic phenol was employed, 3,4-dihydro-2*H*-pyran was formed as a major byproduct.[7]

The stereochemistry of the transacetalization is to be noted. When irradiation of an equimolar mixture of *cis*- or *trans*-6-methyltetrahydropyran-2-yl ether **4** and an alcohol was conducted



in acetonitrile containing phenanthrene and DCNB (10% each), the corresponding transacetalization product **5** was obtained in favor of the trans isomer regardless of the stereochemistry of the starting material **4** (Table II). The observed trans/cis ratio, 8:1–6:1, is contrasted to the thermodynamic ratio, ~6:4.[8] Since the products do not isomerize under the photoreaction conditions, the stereoselectivity is a result of some kinetic control. The trans stereoselection is attributable to the kinetic anomeric effect, which favors the α-side attack of nucleophiles to the cyclic oxocarbenium

(5) Acetals have comparable or somewhat lower oxidation potentials with respect to the corresponding alcohols or ethers.[6] Actually, the phenolic products and the substrates of type **1** react competitively with the sensitizer radical cations such as $P^{+\cdot}$, and hence the conversion appears to level off at the late stage of the reaction.

(6) Ushida, K.; Shida, T. *J. Am. Chem. Soc.* **1982**, *104*, 7332–7333. Symons, M. C. R.; Wren, B. W. *J. Chem. Soc., Perkin Trans. 2* **1984**, 511–522.

(7) Hoz, S.; Aurbach, D. *J. Chem. Soc., Chem. Commun.* **1984**, 364–365.

(8) Anderson, C. B.; Sepp, D. T. *Tetrahedron* **1968**, *24*, 1707–1716.

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

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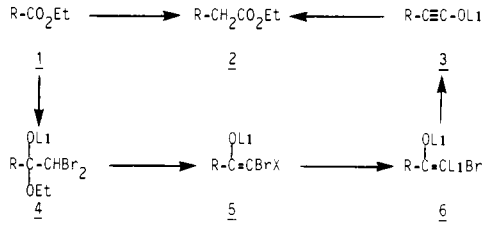
Herein we report on the mechanism, stereochemistry, and scope of a new procedure for the homologation of esters (i.e., **1** → **2**) and its application to the synthesis of the antifungal antibiotic oudemansin (**32**). This method is based upon our previously reported rearrangement reaction[2] of α-halo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

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