of 20% CF_3COOH in CH_2Cl_2 (5 mL) was added to the stirred reaction mixture. After 30 min, the mixture was concentrated to dryness and the resulting solid was dissolved in water (10 mL). The aqueous solution was washed with CH_2Cl_2 (2 × 5 mL) and ether (2 × 5 mL) and then concentrated to give the desired product **15** (0.16 g, 0.33 mmol, 87%). ^{13}C NMR (D_2O, ppm): 88.5 (1′ C), 42.3 (2′ C), 73.8 (3′ C), 89.9 (4′ C), 64.5 (5′ C), 168.7 (4 CO), 154.8 (2 CO), 116.6 (5 C), 141.5 (6 C), 26.2 (7 C), 37.7 (8 C), 41.7 and 42.1 (9 C and 10 C), 34.4 (11 C), 130.0 (12 C), 120.8 (13 C), 136.9 (14 C), 178.7 (15 C), 173.9 (16 C). ^1H NMR (D_2O): δ 6.25 (t, 1 H, H1′, J = 7.0 Hz), 2.35 (m, 2 H, H2′), 4.45 (m, 1 H, H3′), 4.05 (m, 1 H, H4′), 3.8 (m, 2 H, H5′), 7.7 (s, 1 H, H6), 2.5 (m, 4 H, H7 and H8), 3.3 (br s, 4 H, H9 and H10), 3.8 (s, 2 H, H11), 7.4 (s, 1 H, H13), 8.7 (s, 1 H, H14). FABMS m/z 463^+ (M + 2 Li − H), 457^+ (M + Li), 341^+ (M + Li − sugar). Exact mass found 457.2094, calculated for $C_{19}H_{26}N_6O_7Li$ 547.2022.

5′-*O*-[Bis(4-methoxyphenyl)phenylmethyl]-5-[[2-[[2-[[(2,2-dimethylethoxy)carbonyl]amino]-3-[1-[(2,2-dimethylethoxy)carbonyl]-1*H*-imidazol-4-yl]-1-oxopropyl]amino]ethyl]thio]-2′-deoxyuridine (17). 5′-*O*-[Bis(4-methoxyphenyl)phenylmethyl]-5-[(2-aminoethyl)thio]-2′-deoxyuridine (**16**) (1.25 g, 2.07 mmol), Et_3N (0.3 mL, 2 mmol, and Boc-L-his(Boc)-*O*-pfp **4** (1.19 g, 2.5) mmol) were dissolved in CH_2Cl_2 (10 mL) and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was concentrated and chromatographed on a silica gel column eluting with a gradient of 0 to 10% EtOH in CH_2Cl_2. The desired product **17** (1.5 g, 1.59 mmol, 77%) eluted with 8% EtOH in CH_2Cl_2 (R_f −0.52). Mp: 142 °C. ^{13}C NMR ($CDCl_3$, ppm): 85.8, (1′ C), 41.3 (2′ C), 72.3 (3′ C), 86.6 (4′ C), 63.8 (5′ C), 163.4 (4 CO), 150.3 (2 CO), 107.3 (5 C), 145.0 (6 C), 34.9 (7 C), 38.6 (8 C), 54.3 (9 C), 31.3 (10 C), 139.2 (11 C), 114.8 (12 C), 136.9 (13 C), 171.6 (14 C), 87.0 (15 C), 27.9 (16 C), 79.8 (17 C), 28.4 (18 C), 85.7 (19 C), 55.3 (20 C), 155.6, (21 C), 147.0 (22 C). ^1H NMR ($CDCl_3$): δ 6.35 (t, 1 H, H1′, J = 7.0 Hz), 2.4 (m, 2 H, H2′), 4.6 (m, 1 H, H3′), 4.15 (m, 1 H, H4′), 3.45 (m, 2 H, H5′), 3.0 (m, 4 H, H7 and H8), 4.45 (m, 1 H, H9), 3.3 (m, 2 H, H10), 1.6 (s, 9 H, H16), 1.4 (s, 9 H, H18), 3.8 (s, 6 H, H20). FABMS m/z 988^+, (M + Li). Exact mass found 949.3960, calculated for $C_{51}H_{63}N_7O_{13}Li$ 949.3933.

5-[[2-[[2-Amino-3-(1*H*-imidazol-4-yl)-1-oxopropyl]amino]ethyl]thio]-2′-deoxyuridine (18). The nucleoside **17** (0.2 g, 0.212 mmol) was dissolved in CH_2Cl_2 (5 mL), and a solution of 25% CF_3COOH in CH_2Cl_2 (5 mL) was added to the stirred reaction mixture. After 10 min, the mixture was concentrated to dryness. The solid was dissolved in water (10 mL), washed with CH_2Cl_2 (2 × 5 mL) and ether (2 × 5 mL), and concentrated to give the desired product **18** (0.086 g, 0.184 mmol, 87%). ^{13}C NMR (D_2O, ppm): 89.3 (1′ C), 42.4 (2′ C), 73.5 (3′ C), 90.2 (4′ C), 64.3 (5′ C), 167.9 (4 CO), 154.5 (2 CO), 109.5 (5 C), 149.2 (6 C), 36.2 (7 C), 41.6 (8 C), 55.6 (9 C), 29.4 (10 C), 129.3 (11 C), 121.7 (12 C), 137.7 (13 C), 171.1 (14 C). ^1H NMR (D_2O): δ 6.25 (t, 1 H, H1′, J = 7.0 Hz), 2.45 (m, 2 H, H2′), 4.5 (m, 1 H, H3′), 4.05 (m, 1 H, H4′), 3.85 (m, 2 H, H5′), 8.2 (s, 1 H, H6), 2.75 (m, 2 H, H7), 3.35 (m, 2 H, H8), 4.3 (t, 1 H, H9), 3.4 (m, 2 H, H10), 7.45 (s, 1 H, H12), 8.75 (s, 1 H, H13). FABMS m/z 447^+ (M + Li). Exact mass found 447.4694, calculated for $C_{20}H_{29}N_7O_7Li$ 447.4644.

Acknowledgment. We wish to thank Dr. W. B. Wise for his valuable discussions and assistance with the indirect detection, HETCOR, and COSY NMR spectroscopy on compounds **5**, **6**, and **8**; Drs. E. W. Kolodziej and P. C. Toren for mass spectral data; and Ms. A. M. Huber for literature searches and nomenclature.

Supplementary Material Available: NMR spectra of representative compounds and the experimental conditions are given in supplementary material (29 pages). Ordering information is given on any current masthead page.

Organotin-Mediated Monoacylation of Diols with Reversed Chemoselectivity: A Convenient Synthetic Method[1]

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The organotin-mediated monoesterification of unsymmetrical diols with reversed chemoselectivity has been explored to ascertain scope and limits of the method and to provide an easy and convenient synthetic procedure. The reaction has been performed on a set of substituted diols with some acylating agents usually employed as protecting groups. Two different procedures have been devised to obtain either the desired diol monoesters directly or the corresponding trialkylsilyl ethers as protected derivatives. The latter provides a convenient approach to the preparation of easily interconvertible diol monoesters. Also, the reaction has been optimized as a one-pot procedure, avoiding the isolation and purification of the stannylated intermediates. The reversed monoesterification method has been successfully applied to 1,2-, 1,3-, and 1,4-diols of primary–secondary, primary–tertiary, and secondary–tertiary types and to ether functions containing 1,2-diols. Within its limits, the described method represents the first direct one-pot monoesterification of diols at the most substituted site, allowing some remarkable achievements as (a) an almost regiospecific reversed monobenzoylation of some 1,2-diols, (b) the selective acylation of the tertiary hydroxyl of a primary–tertiary diol, and (c) a highly selective preparation of the secondary pivalate of primary–secondary diols.

In a previous paper,[2] we reported experimental evidence that the reactivity order of hydroxyl groups toward acylating agents can be reversed by activation through their stannyl derivatives. In particular, unsymmetrically substituted ethylene glycols could be efficiently esterified at the most substituted site. Such observation was unprecedented in the chemical literature: while chemoselective esterification reactions of diols and polyols,[3] including regioselective manipulation of hydroxyl groups via organotin derivatives,[4] were reported to enhance the natural

(1) Group 14 Organometallic Reagents. 9. Part 8: Mordini, A.; Roelens, S. *J. Org. Chem.* **1989**, *54*, 2643.

(2) Ricci, A.; Roelens, S.; Vannucchi, A. *J. Chem. Soc., Chem. Commun.* **1985**, 1457.

(3) (a) Greene, T. W. *Protective Groups in Organic Synthesis*; Wiley-Interscience: New York, 1981; p 50. (b) Rana, S. S.; Barlow, J. J.; Matta, K. L. *Tetrahedron Lett.* **1981**, *22*, 5007. (c) Mukaiyama, T.; Pai, F. C.; Onaka, M.; Narasaka, K. *Chem. Lett.* **1980**, 563. (d) Posner, G. H.; Oda, M. *Tetrahedron Lett.* **1981**, *22*, 5003. (e) Therisod, M.; Klibanov, A. M. *J. Am. Chem. Soc.* **1986**, *108*, 5638.

(4) David, S.; Hanessian, S. *Tetrahedron* **1985**, *41*, 643–663.

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Table I. Quenching of the Monobenzoylation Reaction of RCHOHCH$_2$OH (Equation 1)[a]

entry	quenching reagent	R	monoester yield, %	mME:lME
1	Me_3SiCl	Me	79	80:20
2	$PhMe_2SiCl$[b]	Me	84	85:15
3	$PhMe_2SiCl$[b]	Ph	90	95:5
4	Et_3SiCl	Me	54	83:17
5	Bu_3SiCl	Me	50	80:20
6	t-$BuMe_2SiCl$	Me	30	60:40
7	H_2O	Ph	89	75:25
8	H_2O/HCl (10:1)	Ph	89	81:19
9	H_2O/HCl (2:1)	Ph	91	82:18
10	$(COOH)_2/CHCl_3$[c]	Ph	85	49:51
11	$(COOH)_2/CH_3CN$	Ph	84	79:21

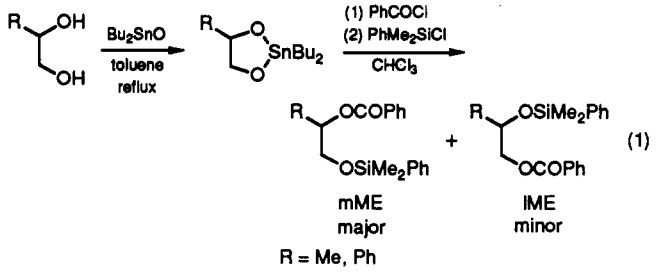
[a] Crystallized dioxastannolanes were used as starting material. [b] Data from ref 2. [c] Incomplete destannylation.

hydroxyl group reactivity, i.e., primary > secondary ≫ tertiary, no reports had been published on reversed selectivity.

Since the above paper, no general method has yet appeared, to our knowledge, to perform the reversed esterification of diols.[5] Because a method of potentially wide application, complementary to known reactions, would be an extremely useful tool for the synthetic chemist, we have explored in this paper the possibility of providing a convenient synthetic procedure, trying to optimize yields and selectivities, and to establish scope and limitations of the organotin-mediated method for the selective monoesterification of diols at the most substituted hydroxyl.

Results and Discussion

As described for the monobenzoylation of 1,2-propanediol and 1-phenyl-1,2-ethanediol,[2] azeotropic dehydration with toluene of the diol in the presence of dibutyltin oxide affords the corresponding dibutylstannylene derivative, which is isolated and purified by crystallization. The dioxastannane is then reacted with 1 equiv of benzoyl chloride in concentrated chloroform solution and subsequently quenched with 1 equiv of phenyldimethylsilyl chloride (eq 1). Besides diesters (DE)



(1)

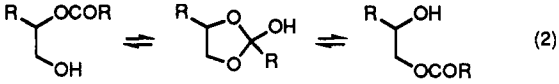
and disilylated starting material (DS), the silyl-protected diol monoester, functionalized at the most substituted hydroxy group (most substituted monoester, mME), is selectively obtained, together with minor amounts of the regioisomeric primary ester (least substituted monoester, lME). The pure mME can then be obtained in most cases by flash column chromatography on silica gel.

Quenching. A preliminary screening of commercial trialkylsilyl chlorides as quenching reagents, analyzing the reaction by ^{1}H NMR spectroscopy, showed best results when the stannylation mixture was quenched with phenyldimethylsilyl chloride ($PhMe_2SiCl$). However, the more convenient trimethylsilyl chloride (Me_3SiCl) gave very good yields and selectivities as well (Table I, entries 1–6).[6]

Destannylation of the acylation mixture can also be achieved by either aqueous or anhydrous direct protonolysis. The latter is conveniently performed in chloroform or acetonitrile solution with oxalic acid, which induces complete precipitation of organotin oxalates. In Table I, the results relative to the neutral or acidic (HCl) aqueous quenching of the benzoylation mixture of 1-phenyl-1,2-ethanediol (entries 7–9) are compared with anhydrous quenching with oxalic acid (entries 10 and 11) and with $PhMe_2SiCl$ (entry 3). As shown, all procedures are efficient, except for protonolysis in chloroform. Quenching in acetonitrile is particularly convenient, in that it allows clean elimination of tin byproducts by simple filtration. It is also a preferable procedure with reactive esters, when hydrolysis might occur during aqueous quenching. Care should be paid to the fact that the stoichiometric amount of added oxalic acid is crucial: It has been verified that a drastic decrease in yields and selectivity is observed for an excess of the latter.

Quenching with trialkylsilyl chlorides is suitable when isomerically stable hydroxy esters are required, for example when products should undergo subsequent transformations. As a control experiment on their stability, two different regioisomeric mixtures of silyl-protected 1- and 2-benzoyl esters of 1,2-propanediol; i.e., 92:8 (from a blank experiment) and 23:77 (from the stannylation method, in the presence of the dibutyltin dichloride formed in the reaction), respectively, showed no detectable isomerization after a 16-h reflux in chloroform.[7] An additional 4-h reflux, after the addition of 50 mol % of the corresponding dioxastannolane, still gave unaltered isomeric ratios.

In this context, it is important to stress that hydroxy esters, in particular monoesters of 1,2-diols, are known to isomerize[8] (eq 2) and that such isomerization is very fast in acidic[9] or alkaline media.[10] While for moderately re-



(2)

active monoesters (e.g., benzoyl esters) equilibration has been verified to be slow, for more reactive ones (e.g., acetyl esters) we have found that partial isomerization occurs during workup. This becomes a serious drawback for hydroxy esters more reactive than acetates, and isolation of pure regioisomers might become a meaningless task. Quenching with trialkylsilyl chlorides provides a practical solution to this problem.

Monobenzoylation of Diols. In the described procedure, the intermediate dioxastannolanes are isolated and purified; this allows clean monobenzoylation with high yields and selectivities. However, since a one-pot reaction is highly desirable, especially in multistep procedures, the method has been further improved, avoiding the isolation of dioxastannanes. Results are generally quite satisfactory (cf. Table I, entry 2, and Table II, entry 1; Tables I and II, entries 3; Table II, entries 8 and 9 and entries 14 and

(5) See, however: Pautard, A. M.; Evans, S. A. *J. Org. Chem.* **1988**, *53*, 2300.

(6) Variable amounts of desilylated products were occasionally found either because of adventitious hydrolysis during workup or because of incomplete quenching, but they never significantly affected the results and were not considered in the reported data, which refer to silyl-protected monoesters only. Thus, figures describing monoester yields often represent lower limiting values.

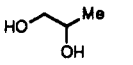
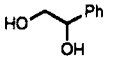
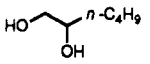
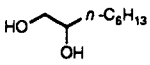
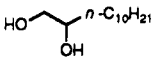
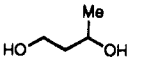
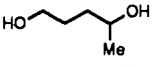
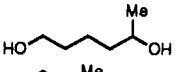
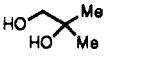
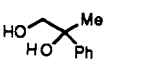
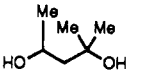
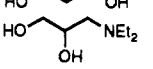
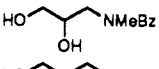
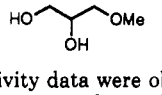
(7) Two largely different compositions were chosen to avoid the possibility of inspecting an already equilibrated mixture of isomers.

(8) (a) Cohen, T.; Dughi, M.; Notaro, V. A.; Pinkus, G. *J. Org. Chem.* **1962**, *27*, 814. (b) Hirano, M.; Morimoto, T. *J. Chem. Soc., Perkin Trans. 2*, **1984**, 1033.

(9) Santry, L. J.; Azer, S.; McClelland, R. A. *J. Am. Chem. Soc.* **1988**, *110*, 2909.

(10) McClelland, R. A.; Seaman, N. E.; Cramm, D. *J. Am. Chem. Soc.* **1984**, *106*, 4511.

Table II. Yields and Conditions for Monobenzoylation of Diols[a]

entry	diol	stannylation time,[b] h	quenching reagent[c]	monoester yield, %	mME:lME	mME isolated yield, %
1		7	$(COOH)_2$	86	78:22	75[d]
2		6	Me_3SiCl	83	98:2[e]	
3		6	$PhMe_2SiCl$	79	95:5	59
4		6	$(COOH)_2$	90	86:14	77
5		21	$(COOH)_2$	84	72:28	53
6		23	$(COOH)_2$	80	72:28	52
7		22	$(COOH)_2$	70	66:34	32
8		7	$PhMe_2SiCl$	80	79:21[e,f]	
9		7	$(COOH)_2$	76	78:22	68[d]
10		20	$PhMe_2SiCl$	61	69:31[e,f]	
11		20	$(COOH)_2$	75	23:77	64[d]
12		24	Me_3SiCl		<5:95	
13		22	$(COOH)_2$		5:95[f]	
14		20	$PhMe_2SiCl$[g]	62	89:11	45[h]
15		20	$PhMe_2SiCl$[g]	60	91:9	
16		20	$(COOH)_2$	95	<1:99	75[i]
17		18	$PhMe_2SiCl$[j]	50	77:23	
18		18	$(COOH)_2$	95	<1:99	95[i]
19		24	Me_3SiCl[m]	92	63:37	
20		24	$(COOH)_2$	77	<1:99	58[i]
21		23	$(COOH)_2$	78	8:92	
22		20	Me_3SiCl	67	12:88	
23		22	$(COOH)_2$	72	7:93	
24		20	Me_3SiCl	72	76:24	
25		23	$(COOH)_2$	94	8:92	

[a] Yield and selectivity data were obtained by ^1H NMR, unless otherwise stated. Values relative to silylated quenching reagents refer to silyl-protected monoesters only, neglecting desilylated derivatives. [b] In refluxing toluene. [c] Unless otherwise stated, destannylation was achieved by stirring the mixture at room temperature for ca. 20 h with oxalic acid and for 1–2 h with silyl chlorides. [d] Regioisomeric mixture. [e] From crystallized dioxastannolane. [f] Determined by GC analysis. [g] Destannylated by refluxing the solution for 18 h. [h] From crystallized dioxastannolane, obtained in 76% yield. [i] Yield of lME. [j] Destannylated by refluxing the solution for 42 h. [m] Destannylated by refluxing the solution for 30 h.

15), and show that, with the exclusion of the purification step, an overall easier and convenient procedure is provided.

Inspection of Table II reveals good to excellent results for 1,2, 1,3, and 1,4 primary–secondary diols (entries 1–10).[11] Satisfactory reversal of chemoselectivity in monobenzoylation could even be achieved with primary–tertiary 1,2-diols (entries 15 and 17) and a secondary–tertiary 1,3-diol (entry 19), for which only the quenching method with trialkylsilyl chlorides was successful. The one-pot procedure is particularly suggested for 1,4-diols and for highly substituted diols, whose stannylene derivatives, at variance with other dioxastannanes, are extremely sensitive to hydrolytic cleavage.[12] Besides hydrolysis, incomplete formation of the dioxastannane, due to steric hindrance or ring strain, might concur to lower yields and selectivities. In such cases, quenching with oxalic acid appears to be an inadequate procedure (entries 11, 16, 18, and 20). Lack of dioxastannane formation is also proposed as a possible explanation for failure in the reversed monobenzoylation, with both quenching procedures, of a 1,5-diol (entries 12 and 13) and of 1,2-diols with nitrogen-containing substituents, that appear to interfere drastically (entries 21–23). Ethereal oxygens in the side chain do not prevent reversed monobenzoylation: Good results were obtained with the methoxymethyl substituent, for which only the quenching with trialkylsilyl chloride was successful (entries 24 and 25).

Some remarkable results should be emphasized: (a) The outstanding selectivity achieved with the 4-phenyl-substituted dioxastannolane (entry 2) shows that in some instances the pure secondary ester can be regioselectively prepared in excellent yields. (b) Direct acylation of a tertiary hydroxy group, normally considered unreactive, can be achieved selectively, even in the presence of a vicinal primary hydroxyl.

Acylation. To further establish the scope of the organotin-mediated reversed monoacylation, esterification of 1-phenyl-1,2-ethanediol has been performed with various commercially available acyl chlorides and with acetic an-

(11) The less satisfactory results obtained with 1,12-dodecanediol (Table II, entry 7) were believed to depend on the surfactant properties of the substrate that appeared to interfere with both the dioxastannolane formation and the esterification reaction. For a recent work related to this subject, see: Otera, J.; Ioka, S.; Nozaki, H. *J. Org. Chem.* **1989**, *54*, 4013.

(12) Poor results (mME:lME = 26:74 for 1,4-pentanediol) or failure in chemoselectivity reversal (mME:lME = 6:94 with Me_3SiCl and <2:98 with $PhMe_2SiCl$ for 2-phenyl-1,2-propanediol) was observed when such substrates were not carefully dried or stored, accidentally producing large amounts of destannylated diols. Such problems were not encountered with the dibutylstannylene derivatives of monosubstituted 1,2-diols, which are insensitive to moisture and indefinitely stable.

Table III. Yields and Conditions for the Acylation of 1-Phenyl-1,2-ethanediol[a]

acylating agent	acylation time, min	temp, °C	monoester yield,[b,c] %	*m*ME:*l*ME[c]
benzoyl chloride	60	25	83	98:2
2-chlorobenzoyl chloride	15	25	75	93:7
4-methoxybenzoyl chloride	15	25	48[d]	71:29
acetyl chloride	10	−25	69	93:7
	10	0	63	96:4
	5	−25	83[e]	71:29
methoxyacetyl chloride	5	−78	66	95:5
pivaloyl chloride	60	25	79	94:6
acetic anhydride[e]	10	−60	47	57:43
	10	−25	43	42:58
	24 h	25	<2[f]	

[a] Reaction performed on the crystallized dioxastannolane and quenched with trimethylsilyl chloride unless otherwise stated. [b] Remaining products are starting materials and bifunctionalized derivatives. [c] Data relative to silylated products only. [d] Use of the unpurified commercial reagent caused extensive hydrolysis (22% yield of unsilylated hydroxyesters). [e] Quenched with oxalic acid: isomerizes on standing. [f] Complete diesterification.

hydride, commonly employed as protecting agents, starting from the crystallized dioxastannolane. Results and experimental conditions are collected in Table III (data for benzoylation have been reported for direct comparison). It is seen that the method can be extended to other protecting groups by choosing the appropriate conditions. Unsatisfactory acetylation has been obtained with acetic anhydride, for which the destannylation procedure with Me_3SiCl was unsuccessful: Poor results could thus be due to inappropriate but unavoidable quenching with oxalic acid. Good yields and excellent selectivities are instead obtained with acetyl chloride, which is the reagent of choice. To avoid extensive diester formation, more reactive acylating agents require lower temperature and shorter reaction times, as exemplified by methoxyacetyl chloride.[13] Conversely, the unreactive pivaloyl chloride affords excellent reversed monoacylation, without taking any particular care with experimental conditions. It is noteworthy that pivaloyl chloride is normally used for selective protection of primary hydroxyl groups[14,15] because of its inertness toward secondary hydroxyls; thus, in this case, the stannylation method represents a unique tool to perform a complete reversal of the natural hydroxy group reactivity.

In conclusion, even with some limitations, reversal of chemoselectivity is quite generally achieved. The present method can be usefully employed for easy and direct access to diols monoacylated at the most substituted site. Investigation on the origin and the mechanism of this chemoselectivity reversal is in progress and will be reported in a forthcoming paper.

Experimental Section

Materials, Instruments, and Techniques. The general preparation and purification of dioxastannolanes and chloroform, as well as experimental details on the reaction, have been described in previous papers.[2,16,17] All the starting diols, except for 2-methyl-1,2-propanediol prepared as described below and the acylating and silylating reagents, were commercial samples purified by fractional distillation. The anhydrous, ethanol-free chloroform was kept in the dark over 13X activated molecular sieves. $CDCl_3$ (Merck, 99.8%) stored on Ag foil and 13X-activated molecular sieves was used for reactions and NMR spectra. Acetonitrile and toluene (Carlo Erba, RPE-ACS) were stored over 3-Å activated molecular sieves. Melting and boiling points are uncorrected. ^1H NMR spectra at 300 and 90 MHz were obtained on Varian VXR 300 and EM 390 instruments, respectively; δ values (from Me_4Si with $CHCl_3$ as internal secondary reference at δ 7.26) refer to specific compounds detected directly in the reaction mixture. ^1H NMR data (digital resolution 0.001 ppm, PW < 30°, 3.8-s acquisition, 10-s repetition rate) are reported only for signals that have been used for the identification and the analysis of products. Regioisomers were assigned by acylation-induced chemical shifts and by comparison with mixtures obtained following literature procedures in blank experiments. EI mass spectra were obtained at 70 eV on a GC–MS apparatus HP-5790 A/HP-5970 A mass-selective detector, equipped with a high-performance dimethylsilicone fluid capillary 25-m column, operating with He carrier at 9-psi head pressure. Microanalyses were performed with a Perkin-Elmer 240 C elemental analyzer. Products were isolated by flash chromatography on silica gel 60 (Merck, 230–400 mesh) columns, 20 cm × 40 mm, or by centrifugal radial thin-layer chromatography on a 2-mm layer of silica gel.

General Acylation Procedure. A 1.5-mmol portion of the diol was dissolved or suspended in 30 mL of toluene, and after the addition of dibutyltin oxide in 5% molar excess, water was separated by azeotropic distillation in a Dean–Stark apparatus for a variable length of time, depending on the substrate (see Table II). After evaporation of the solvent, the residue was dried under vacuum, dissolved under nitrogen in 1.5 mL of anhydrous $CHCl_3$, and cooled to 0–5 °C. An equimolar amount of the appropriate acylating reagent in 1 mL of the same solvent was added dropwise with a syringe through a septum cap to the stirred solution, and the reaction mixture was then allowed to react at room temperature for 1 h (except otherwise stated), after which was quenched according to two different methods.

Method A. Quenching with Trialkylsilyl Chlorides. The solution was cooled to 0–5 °C, added dropwise with a syringe of a solution of the appropriate silyl chloride (5% molar excess) in 1 mL of anhydrous $CHCl_3$, and then allowed to react at room temperature for 1–2 h, except otherwise stated. The mixture obtained was then analyzed by ^1H NMR spectroscopy.

Method B. Quenching with Oxalic Acid. The solvent was evaporated under vacuum, and the residue was dissolved in 8 mL of anhydrous CH_3CN. The solution was cooled to 0–5 °C, 0.75 mmol of oxalic acid in 3.5 mL of CH_3CN was added, and the mixture was stirred at room temperature for 20 h, except otherwise stated. The resulting suspension was filtered under nitrogen, and the solid was washed several times with CH_3CN. The residue obtained after evaporation of the solvent under vacuum was dissolved in $CDCl_3$ and the mixture analyzed by ^1H NMR spectroscopy.

Reactions for the acylation of 1-phenyl-1,2-ethanediol (Table III) were carried out on the crystallized dioxastannolane in 5-mm NMR tubes by mixing appropriate volumes of 0.7–1 M solutions of the starting materials and 1.5–2 M solutions of the reagents in anhydrous $CDCl_3$ with a syringe through a septum cap according to the above general procedure.

Reaction of 1,2-Propanediol with Benzoyl Chloride. 1,2-Propanediol (145 mg, 1.90 mmol) was reacted with dibutyltin oxide (499 mg, 2.00 mmol) and benzoyl chloride (267 mg, 1.90 mmol). After being quenched with oxalic acid (86 mg, 0.95 mmol) according to method B, 364 mg of crude mixture was obtained, which was analyzed (Table II, entry 1) by ^1H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABM part of an $ABMX_3$ system): (mME) AB 3.73–3.84 (m, 2 H), M 5.25 (m, 1 H), (lME) AB 4.16–4.24 (m, 2 H), M 4.35 (m, 1 H), (DE) AB 4.42–4.54 (m, 2 H), M 5.54 (m, 1 H), (1,2-propanediol) A 3.34–3.42 (m, 1 H), B 3.59–3.64 (m, 1 H), M 3.89 (m, 1 H). Separation by centrifugal radial thin-layer chromatography, using petroleum ether/ethyl acetate (92:8) as eluant, afforded 255 mg of a regioisomeric mixture (mME + lME) in 75% total yield.

1,2-Propanediol 2-*O*-benzoyl ester: oil; GC (program 50 °C (2 min), 15 °C/min to 280 °C) t_R 10.76 (lME 11.44); MS (EI) *m/z*

(13) Reagent for selective protection–deprotection of primary hydroxy groups: Reese, C. B.; Stewart, J. C. M. *Tetrahedron Lett.* **1968**, 4273.
(14) Griffin, B. E.; Jarman, M.; Reese, C. B. *Tetrahedron* **1968**, *24*, 639.
(15) Robins, M. J.; Hawrelak, S. D.; Kanai, T.; Siefert, J. M.; Mengel, R. *J. Org. Chem.* **1979**, *44*, 1317.
(16) Luchinat, C.; Roelens, S. *J. Am. Chem. Soc.* **1986**, *108*, 4873.
(17) Roelens, S. *J. Chem. Soc., Perkin Trans. 2* **1988**, 2105.

(relative intensity) 162 (2), 136 (19), 135 (13), 123 (15), 105 (100), 92 (13), 91 (10), 77 (72), 58 (11), 51 (40), 45 (16). Anal. Calcd for $C_{10}H_{12}O_3$ (regioisomeric mixture): C, 66.65; H, 6.71. Found: C, 66.88; H, 6.93.

Reactions of 1-Phenyl-1,2-ethanediol with Benzoyl Chloride. (a) 4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane (111 mg, 0.30 mmol) was reacted in a 5-mm NMR tube with benzoyl chloride (42 mg, 0.30 mmol) at room temperature for 1 h. After being quenched with trimethylsilyl chloride (34 mg, 0.31 mmol) according to method A, the reaction mixture was analyzed (Table II, entry 2) by GC–MS and ^1H NMR: GC (SE 30, 30 m; program 80 °C (3 min), 5 °C/min to 280 °C) (mME) t_R 33.78, MS (EI) m/z (relative intensity) 192 (12), 179 (16), 105 (100), 103 (12), 91 (15), 77 (33), 73 (31), 51 (11), 45 (11), (lME) t_R 33.24, MS (EI) m/z (relative intensity) 180 (17), 179 (100), 105 (52), 91 (14), 77 (51), 75 (20), 73 (69), 51 (17), 45 (22); ^1H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABX)) (mME) A 3.89–3.94 (m, 1 H), B 4.00–4.06 (m, 1 H), X 6.10 (m, 1 H), (lME) AB 4.32–4.45 (m, 2 H), X 5.08 (m, 1 H), (DE) AB 4.67–4.82 (m, 2 H), X 6.45 (m, 1 H), (DS) AB 3.57–3.68 (m, 2 H), X 4.73 (m, 1 H).

(b) 1-Phenyl-1,2-ethanediol (209 mg, 1.51 mmol) was reacted with dibutyltin oxide (395 mg, 1.59 mmol) and benzoyl chloride (210 mg, 1.49 mmol). After the mixture was quenched with phenyldimethylsilyl chloride (271 mg, 1.59 mmol) according to method A, 1.02 g of crude mixture was obtained and analyzed (Table II, entry 3) by ^1H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABX)): (mME) A 3.95–4.00 (m, 1 H), B 4.06–4.12 (m, 1 H), X 6.18 (m, 1 H), (lME) AB 4.42–4.52 (m, 2 H), X 5.15 (m, 1 H), (DE) AB 4.73–4.88 (m, 2 H), X 6.51 (m, 1 H), (DS) A 3.63–3.69 (m, 1 H), B 3.73–3.81 (m, 1 H), X 4.82 (m, 1 H). A 408-mg portion of the mixture was separated by flash column chromatography, with petroleum ether/ethyl acetate (90:10) as eluant, to afford 134 mg of pure mME in 59% yield.

1-Phenyl-1,2-ethanediol 1-*O*-benzoyl ester 2-dimethylphenylsilyl ether: oil; MS (EI) m/z (relative intensity) 255 (12), 241 (54), 179 (29), 165 (15), 135 (54), 105 (100), 77 (30). Anal. Calcd for $C_{23}H_{24}O_3Si$: C, 73.37; H, 6.42. Found: C, 73.62; H, 6.20.

(c) 1-Phenyl-1,2-ethanediol (210 mg, 1.52 mmol) was reacted with dibutyltin oxide (395 mg, 1.60 mmol) and benzoyl chloride (215 mg, 1.52 mmol). After the mixture was quenched with oxalic acid (68 mg, 0.76 mmol) according to method B, 382 mg of crude mixture was obtained, which was analyzed (Table II, entry 4) by ^1H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABX)): (mME) AB 3.91–4.10 (m, 2 H, coupled to OH), X 6.12 (m, 1 H), (lME) A 4.40–4.48 (m, 1 H), B 4.52–4.57 (m, 1 H), X 5.12 (m, 1 H, coupled to OH), (DE) AB 4.64–4.79 (m, 2 H), X 6.42 (m, 1 H), (1-phenyl-1,2-ethanediol) A 3.64–3.72 (m, 1 H), B 3.76–3.82 (m, 1 H), X 4.84 (m, 1 H). Separation of the mixture by centrifugal radial thin-layer chromatography, with petroleum ether/ethyl acetate (92:8) as eluant, gave 284 mg of pure mME in 77% yield.

1-Phenyl-1,2-ethanediol 1-*O*-benzoyl ester: solid; mp 65–67 °C; MS (EI) m/z (relative intensity) 224 (7), 120 (11), 107 (11), 105 (100), 76 (31), 51 (11), 43 (14). Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found: C, 74.57; H, 5.62.

Reaction of 1,2-Hexanediol with Benzoyl Chloride. 1,2-Hexanediol (178 mg, 1.50 mmol) was reacted with dibutyltin oxide (393 mg, 1.58 mmol) and benzoyl chloride (212 mg, 1.50 mmol). After the mixture was quenched with oxalic acid (68 mg, 0.75 mmol) according to method B, 357 mg of crude mixture was obtained, which was analyzed (Table II, entry 5) by ^1H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABM part of an $ABMX_2$ system)): (mME) AB 3.74–3.87 (m, 2 H), M 5.17 (m, 1 H), (lME) A 4.20–4.26 (m, 1 H), B 4.38–4.43 (m, 1 H), M 4.09 (m, 1 H), (DE) A 4.44–4.50 (m, 1 H), B 4.53–4.59 (m, 1 H), M 5.51 (m, 1 H), (1,2-hexanediol) A 3.40–3.47 (m, 1 H), B 3.64–3.71 (m, 1 H), M 3.71 (m, 1 H). Separation of the mixture by flash column chromatography, with petroleum ether/ethyl acetate (70:30) as eluant, afforded 176 mg of pure mME in 53% yield.

1,2-Hexanediol 2-*O*-benzoyl ester: oil; MS (EI) m/z (relative intensity) 136 (27), 135 (28), 106 (10), 105 (100), 92 (21), 91 (12), 77 (32), 51 (11). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.03; H, 8.29.

Reaction of 1,2-Octanediol with Benzoyl Chloride. 1,2-Octanediol (219 mg, 1.50 mmol) was reacted with dibutyltin oxide (393 mg, 1.58 mmol) and benzoyl chloride (212 mg, 1.50 mmol). After the mixture was quenched with oxalic acid (68 mg, 0.75 mmol) according to method B, 393 mg of crude mixture was obtained, which was analyzed (Table II, entry 6) by ^1H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABM part of an $ABMX_2$ system)): (mME) AB 3.74–3.88 (m, 2 H), M 5.18 (m, 1 H), (lME) A 4.21–4.27 (m, 1 H), B 4.39–4.43 (m, 1 H), M 4.00 (m, 1 H), (DE) A 4.44–4.50 (m, 1 H), B 4.54–4.59 (m, 1 H), M 5.50 (m, 1 H), (1,2-octanediol) A 3.41–3.48 (m, 1 H), B 3.67 (br m, 1 H), M 3.72 (m, 1 H). After separation by flash column chromatography, with petroleum ether/ethyl acetate (70:30) as eluant, 196 mg of pure mME was obtained in 52% yield.

1,2-Octanediol 2-*O*-benzoyl ester: oil; MS (EI) m/z (relative intensity) 136 (20), 135 (18), 105 (100), 92 (18), 77 (28), 43 (10), 41 (11), 29 (10). Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.20; H, 8.95.

Reaction of 1,2-Dodecanediol with Benzoyl Chloride. 1,2-Dodecanediol (303 mg, 1.50 mmol) was reacted with dibutyltin oxide (393 mg, 1.58 mmol) and benzoyl chloride (212 mg, 1.51 mmol). After the reaction was quenched with oxalic acid (68 mg, 0.76 mmol) according to method B, 478 mg of crude mixture was obtained and analyzed (Table II, entry 7) by ^1H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABM part of an $ABMX_2$ system)): (mME) AB 3.74–3.88 (m, 2 H), M 5.17 (m, 1 H), (lME) A 4.20–4.26 (m, 1 H), B 4.38–4.43 (m, 1 H), M 3.99 (m, 1 H), (DE) A 4.44–4.50 (m, 1 H), B 4.53–4.59 (m, 1 H), M 5.50 (m, 1 H), (1,2-dodecanediol) A 3.40–3.48 (m, 1 H), B 3.63–3.71 (m, 1 H), M 3.71 (m, 1 H). Separation of the mixture by flash column chromatography, with petroleum ether/ethyl acetate (70:30) as eluant, afforded 146 mg of pure mME in 32% yield.

1,2-Dodecanediol 2-*O*-benzoyl ester: oil; MS (EI) m/z (relative intensity) 207 (36), 136 (31), 135 (21), 123 (11), 105 (100), 92 (19), 77 (18), 43 (14). Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.18; H, 10.01.

Reactions of 1,3-Butanediol with Benzoyl Chloride. (a) 4-Methyl-2,2-dibutyl-1,3,2-dioxastannidine (1.002 g, 3.12 mmol), prepared according to the general procedure described for dioxastannolanes (crystallized from toluene; 71% yield; mp 102–104 °C; ^1H NMR (90 MHz, $CDCl_3$, δ) CH_2O, CHO 3.6–4.3 (br m, 3 H), CH_3 1.1 (d, 3 H), CH_2, C_4H_9 0.7–1.8 (br m, 20 H). Anal. Calcd for $C_{12}H_{26}O_2Sn$: C, 44.90; H, 8.16. Found: C, 45.13; H, 8.23), was reacted with benzoyl chloride (439 mg, 3.12 mmol). After being quenched with phenyldimethylsilyl chloride (560 mg, 3.28 mmol) according to method A, the reaction mixture was analyzed (Table II, entry 8) by GC–MS (program 80 °C (3 min), 10 °C/min to 140 °C, 5 °C/min to 250 °C): (mME) t_R 26.22 min, MS (EI) m/z (relative intensity) 313 (4), 241 (49), 197 (17), 181 (28), 179 (34), 137 (14), 135 (28), 105 (100), 77 (44), 51 (12); (lME) t_R 26.66 min, MS (EI) m/z (relative intensity) 313 (4), 135 (20), 105 (100), 77 (21); (DE) t_R 28.42 min, MS (EI) m/z (relative intensity) 207 (11), 105 (100), 77 (27); (DS) t_R 25.08 min, MS (EI) m/z (relative intensity) 343 (5), 271 (25), 211 (20), 195 (27), 193 (56), 179 (14), 135 (100), 133 (24), 132 (23), 121 (12), 117 (26), 105 (37), 91 (42), 75 (55), 45 (15), 43 (15).

1,3-Butanediol 3-*O*-benzoyl ester 1-dimethylphenylsilyl ether: ^1H NMR (90 MHz, $CDCl_3$, δ) OCH_2 3.71 (app t, 2 H), CHO 5.30 (app sext, 1 H).

(b) 1,3-Butanediol (146 mg, 1.62 mmol) was reacted with dibutyltin oxide (423 mg, 1.70 mmol) and benzoyl chloride (228 mg, 1.62 mmol). After the mixture was quenched with oxalic acid (73 mg, 0.81 mmol) according to method B, 344 mg of crude mixture was obtained, which was analyzed (Table II, entry 9) by ^1H NMR (300 MHz, $CDCl_3$, δ): (mME) CH_2O 3.60–3.76 (m, 2 H), CHO 5.38 (m, 1 H), (lME) CH_2O 4.34–4.42 (m, 1 H), 4.56–4.65 (m, 1 H), CHO 3.98 (m, 1 H), (DE) CH_2O 4.38–4.55 (m, 2 H), CHO 5.40 (m, 1 H), (1,3-butanediol) CH_2O 3.83–3.97 (m, 2 H), CHO 4.12 (m, 1 H). Separation of the mixture by centrifugal thin-layer chromatography, using petroleum ether/ethyl acetate (92:8) as eluant, afforded 214 mg of a mixture of mME + lME in 68% total yield.

1,3-Butanediol 3-*O*-benzoyl ester: oil; GC (program 50 °C (2 min), 10 °C/min to 280 °C) t_R 15.04 (lME 15.30); MS (EI) m/z (relative intensity) 176 (1), 123 (51), 122 (13), 105 (100), 77 (36), 51 (15), 43 (13). Anal. Calcd for $C_{11}H_{14}O_3$ (regioisomeric mixture):

C, 68.02; H, 7.27. Found: C, 68.25; H, 7.20.

Reactions of 1,4-Pentanediol with Benzoyl Chloride. (a) 4-Methyl-2,2-dibutyl-1,3,2-dioxastannepane (1.120 g, 3.34 mmol), prepared according to the general procedure described for dioxastannolanes (oil; ^{1}H NMR (90 MHz, $CDCl_3$, δ) CH_2O, CHO 3.5–4.3 (br m, 3 H), CH_3 1.2 (br d, 3 H), CH_2CH_2, C_4H_9 0.7–2.1 (br m, 22 H). Anal. Calcd for $C_{13}H_{28}O_2Sn$: C, 46.60; H, 8.42. Found: C, 46.73; H, 8.43), was reacted with benzoyl chloride (470 mg, 3.34 mmol). After being quenched with phenyldimethylsilyl chloride (600 mg, 3.51 mmol) according to method A, the reaction mixture was analyzed (Table II, entry 10) by GC–MS (program 80 °C (3 min), 10 °C/min to 140 °C, 5 °C/min to 250 °C): (mME) t_R 28.24 min, MS (EI) m/z (relative intensity) 265 (6), 249 (20), 242 (20), 241 (100), 197 (13), 181 (19), 179 (34), 137 (13), 135 (23), 105 (47), 77 (15); (lME) t_R 28.64 min, MS (EI) m/z (relative intensity) 227 (11), 265 (11), 241 (56), 181 (12), 179 (26), 137 (13), 135 (58), 105 (100), 77 (20), 76 (18); (DE) t_R 29.94 min, MS (EI) m/z (relative intensity) 207 (8), 105 (100), 77 (25), 68 (19); (DS) t_R 27.12 min, MS (EI) m/z (relative intensity) 272 (10), 271 (35), 211 (21), 207 (16), 195 (18), 194 (10), 193 (33), 192 (17), 180 (12), 179 (45), 178 (44), 163 (10), 137 (24), 136 (11), 135 (100), 133 (13), 118 (10), 105 (26), 104 (19), 91 (11), 75 (23), 45 (10), 43 (13), 41 (10).

1,4-Pentanediol 4-*O*-benzoyl ester 1-dimethylphenylsilyl ether: ^{1}H NMR (300 MHz, $CDCl_3$, δ) CH_2O 3.63 (t, 2 H, J = 6 Hz), CHO 5.18 (m, 1 H).

(b) 1,4-Pentanediol (159 mg, 1.53 mmol) was reacted with dibutyltin oxide (399 mg, 1.60 mmol) and benzoyl chloride (213 mg, 1.51 mmol). After the reaction was quenched with oxalic acid (69 mg, 0.77 mmol) according to method B, 341 mg of crude mixture was obtained, which was analyzed (Table II, entry 11) by ^{1}H NMR (300 MHz, $CDCl_3$, δ): (mME) CH_2O 3.69 (t, 2 H, J = 6 Hz), CHO 5.20 (m, 1 H), (lME) CH_2O 4.35 (t, 2 H, J = 6 Hz), CHO 3.89 (app sext, 1 H, J = 6 Hz), (DE) CH_2O 4.34–4.39 (m, 2 H), CHO 5.25 (m, 1 H), (1,4-pentanediol) CH_2O 3.55–3.69 (m, 2 H), CHO 3.81 (m, 1 H). After separation of the mixture by centrifugal radial chromatography, with petroleum ether/ethyl acetate (80:20) as eluant, 203 mg of an isomeric mixture of mME + lME was obtained in 64% total yield.

1,4-Pentanediol 4-*O*-benzoyl ester: oil; GC (program 50 °C (2 min), 10 °C/min to 280 °C) t_R 15.50 (lME 15.62); MS (EI) m/z (relative intensity) 123 (52), 105 (100), 77 (29), 51 (12), 41 (13). Anal. Calcd for $C_{12}H_{16}O_3$ (regioisomeric mixture): C, 69.21; H, 7.74. Found: C, 69.53; H, 7.91.

Reactions of 1,5-Hexanediol with Benzoyl Chloride. (a) 1,5-Hexanediol (83 mg, 1.55 mmol) was reacted with dibutyltin oxide (405 mg, 1.63 mmol) and benzoyl chloride (218 mg, 1.55 mmol). After the reaction was quenched with trimethylsilyl chloride (178 mg, 1.64 mmol) according to method A, it was analyzed (Table II, entry 12) by ^{1}H NMR (300 MHz, $CDCl_3$, δ) (mME) CH_2O 3.50–3.61 (m, 2 H, overlapped with DS), CHO 5.14 (m, 1 H), (lME) CH_2O 4.25 (t, 2 H, J = 7 Hz), CHO 3.76 (m, 1 H), (DE) CH_2O 4.25 (t, 2 H, J = 7 Hz), CHO 5.12 (m, 1 H), (DS) CH_2O 3.50–3.61 (m, 2 H, overlapped with mME), CHO 3.72 (m, 1 H).

(b) 1,5-Hexanediol (177 mg, 1.50 mmol) was reacted with dibutyltin oxide (392 mg, 1.57 mmol) and benzoyl chloride (211 mg, 1.50 mmol). After the reaction was quenched with oxalic acid (68 mg, 0.76 mmol) according to method B, it was analyzed (Table II, entry 13) by GC and ^{1}H NMR: GC (program 50 °C (2 min), 2 °C/min to 200 °C, 10 °C/min to 280 °C) t_R (mME) 52.22, (lME) 53.08; ^{1}H NMR (300 MHz, $CDCl_3$, δ) (mME) CH_2O 3.64 (t, 2 H, J = 7 Hz), CHO 5.19 (m, 1 H), (lME) CH_2O 4.33 (t, 2 H, J = 7 Hz), CHO 3.83 (m, 1 H), (DE) CH_2O 4.32 (t, 2 H, J = 7 Hz), CHO 5.17 (m, 1 H), (1,5-hexanediol) CH_2O 3.66 (t, 2 H, J = 6 Hz), CHO 3.81 (m, 1 H).

Reactions of 2-Methyl-1,2-propanediol with Benzoyl Chloride. Preparation of 1-[(Trimethylsilyl)oxy]-2-methyl-2-propanol. Hydroxyacetone (30.11 g, 406 mmol) was dissolved in 160 mL of benzene together with pyridine (32.15 g, 406 mmol), and after the mixture was cooled to 0–5 °C, a solution of trimethylsilyl chloride (46.37 g, 427 mmol) in benzene was added. The mixture was allowed to react at room temperature for 4 h and filtered, and after evaporation of the solvent, the residue was distilled under reduced pressure, affording a pure fraction containing 29.29 g (50%) of 1-[(trimethylsilyl)oxy]-propan-2-one: liquid; bp 39 °C (9.5 mbar); ^{1}H NMR (90 MHz, $CDCl_3$, δ) $(CH_3)_3$ 0.05 (s, 9 H), CH_3 2.02 (s, 3 H), CH_2O 4.05 (s, 2 H). Of the latter 16.96 g (116 mmol) was dissolved in 200 mL of THF freshly distilled over $LiAlH_4$ and cooled at −78 °C, and a 1.6 M solution of MeLi in diethyl ether (76 mL, 122 mmol) was added. The reaction mixture was then allowed to react for 48 h at room temperature, hydrolyzed with an NH_4Cl-saturated solution, and dried over Na_2SO_4. After evaporation of the solvent, 12.06 g of residue was obtained which, after distillation under reduced pressure, afforded 7.09 g (38%) of pure 1-[(trimethylsilyl)oxy]-2-methyl-2-propanol: liquid; bp 35 °C (6 mbar); ^{1}H NMR (90 MHz, $CDCl_3$, δ) $(CH_3)_3$ 0.22 (s, 9 H), $(CH_3)_2$ 1.25 (s, 6 H), OH 2.57 (s, 1 H), CH_2O 3.43 (s, 2 H); MS (EI) m/z (relative intensity) 147 (25), 131 (27), 104 (4), 89 (22), 75 (81), 73 (69), 59 (100), 47 (11), 45 (30), 43 (30). It has been used as starting material for the monoesterification.

(a) 1-[(Trimethylsilyl)oxy]-2-methyl-2-propanol (648 mg, 3.99 mmol) was reacted with dibutyltin oxide (1.043 g, 4.19 mmol) to afford, after purification according to the general procedure, 4,4-dimethyl-2,2-dibutyl-1,3,2-dioxastannolane in 76% yield. Of the latter 970 mg (3.02 mmol) was reacted with benzoyl chloride (425 mg, 3.02 mmol) and the mixture quenched with phenyldimethylsilyl chloride (541 mg, 3.17 mmol) for 18 h at reflux according to method A, to give 1.920 g of crude mixture, which was analyzed (Table II, entry 14) by ^{1}H NMR (90 MHz, $CDCl_3$, δ(CH_2O)): (mME) 3.88 (s, 2 H), (lME) 4.15 (s, 2 H), (DE) 4.60 (s, 2 H), (DS) 3.35 (s, 2 H). Of the mixture 960 mg was separated by flash column chromatography, with petroleum ether/ethyl acetate (95:5) as eluant, to give 221 mg of pure mME in 45% yield.

2-Methyl-1,2-propanediol 2-*O*-benzoyl ester 1-dimethylphenylsilyl ether: oil; MS (EI) m/z (relative intensity) 255 (17), 242 (20), 241 (100), 206 (22), 197 (10), 179 (37), 135 (44), 105 (73), 77 (20). Anal. Calcd for $C_{19}H_{24}O_3Si$: C, 69.47; H, 7.36. Found: C, 69.32; H, 7.54.

(b) 2-Methyl-1,2-propanediol (134 mg, 1.49 mmol), obtained from 1-[(trimethylsilyl)oxy]-2-methyl-2-propanol by acidic hydrolysis (HCl), was reacted with dibutyltin oxide (389 mg, 1.56 mmol) and benzoyl chloride (210 mg, 1.49 mmol). After the reaction was quenched with oxalic acid (68 mg, 0.75 mmol) according to method B, 305 mg of crude mixture was obtained and analyzed (Table II, entry 16) by ^{1}H NMR (300 MHz, $CDCl_3$, δ(CH_2O)) (mME) 3.78 (s, 2 H), (lME) 4.22 (s, 2 H), (2-methyl-1,2-propanediol) 3.41 (s, 2 H). Separation of the mixture by centrifugal radial thin-layer chromatography, with petroleum ether/ethyl acetate (92:8) as eluant, gave 216 mg of pure lME in 75% yield.

Reactions of 2-Phenyl-1,2-propanediol with Benzoyl Chloride. (a) 2-Phenyl-1,2-propanediol (306 mg, 2.01 mmol) was reacted with dibutyltin oxide (525 mg, 2.11 mmol) and benzoyl chloride (283 mg, 2.01 mmol). After the reaction was quenched with phenyldimethylsilyl chloride (360 mg, 2.11 mmol) for 42 h at reflux according to method A, 1.352 g of crude mixture was obtained, which was analyzed (Table II, entry 17) by GC–MS and ^{1}H NMR: GC–MS (program 80 °C (3 min), 10 °C/min to 140 °C, 5 °C/min to 250 °C) (mME) t_R 28.18 min, MS (EI) m/z (relative intensity) 360 (1), 268 (13), 255 (14), 241 (10), 225 (4), 165 (7), 135 (46), 105 (100), 77 (21); (lME) t_R 28.66 min, MS (EI) m/z (relative intensity) 256 (18), 255 (84), 241 (16), 136 (13), 135 (100), 105 (40), 77 (18); ^{1}H NMR (90 MHz, $CDCl_3$, δ(CH_2O) (AB)): (mME) A 3.93, B 4.11 (2 H, J = 11 Hz), (lME) A 4.78, B 5.00 (2 H, J = 13 Hz).

(b) 2-Phenyl-1,2-propanediol (230 mg, 1.51 mmol) was reacted with dibutyltin oxide (394 mg, 1.59 mmol) and benzoyl chloride (212 mg, 1.51 mmol). After the reaction was quenched with oxalic acid (68 mg, 0.75 mmol) according to method B, 401 mg of crude mixture was obtained and analyzed (Table II, entry 18) by ^{1}H NMR (300 MHz, $CDCl_3$): (δ(CH_2O) (AB)) (mME) A 3.88, B 4.09 (2 H, J = 13 Hz), (lME) AB 4.46–4.55 (2 H, J = 12 Hz), (2-phenyl-1,2-propanediol) (δ(CH_2OH) (ABX)) A 3.62–3.68 (m, 1 H), B 3.79–3.85 (m, 1 H), X 1.69 (m, 1 H). Separation of the mixture by centrifugal radial thin-layer chromatography, with petroleum ether/ethyl acetate (92:8) as eluant, afforded 367 mg of pure lME in 95% yield.

Reactions of 2-Methyl-2,4-pentanediol with Benzoyl Chloride. (a) 2-Methyl-2,4-pentanediol (177 mg, 1.50 mmol) was reacted with dibutyltin oxide (393 mg, 1.58 mmol) and benzoyl

chloride (211 mg, 1.50 mmol). After the reaction was quenched with trimethylsilyl chloride (172 mg, 1.58 mmol) for 30 h at reflux according to method A, it was analyzed (Table II, entry 19) by ^{1}H NMR (300 MHz, $CDCl_3$, δ(CHO)): (mME) 4.77–4.83 (m, 1 H), (lME) 5.28–5.38 (m, 1 H), (DE) 5.46–5.55 (m, 1 H), (DS) 3.64–3.72 (m, 1 H).

(b) 2-Methyl-2,4-pentanediol (177 mg, 1.50 mmol) was reacted with dibutyltin oxide (392 mg, 1.58 mmol) and benzoyl chloride (211 mg, 1.50 mmol). After the reaction was quenched with oxalic acid (68 mg, 0.75 mmol) according to method B, 377 mg of crude mixture was obtained, which was analyzed (Table II, entry 20) by ^{1}H NMR (300 MHz, $CDCl_3$, δ(CHO)): (mME) 4.78–4.82 (m, 1 H), (lME) 5.37–5.48 (m, 1 H), (DE) 5.46–5.56 (m, 1 H), (2-methyl-2,4-pentanediol) 4.18–4.29 (m, 1 H). After separation of the mixture by centrifugal radial thin-layer chromatography, with petroleum ether/ethyl acetate (92:8) as eluant, 195 mg of pure lME was obtained in 58% yield.

Reaction of 3-(Diethylamino)-1,2-propanediol with Benzoyl Chloride. 3-(Diethylamino)-1,2-propanediol (225 mg, 1.53 mmol) was reacted with dibutyltin oxide (400 mg, 1.61 mmol) and benzoyl chloride (215 mg, 1.53 mmol). The reaction was quenched with oxalic acid (69 mg, 0.77 mmol) according to method B and then washed with a Na_2CO_3-saturated solution. After the solution was washed several times with water and dried over anhydrous Na_2SO_4, 407 mg of crude mixture was obtained and analyzed (Table II, entry 21) by ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABM part of an ABMXY system)): (mME) AB 3.92–3.99 (m, 2 H), M 5.20 (m, 1 H), (lME) A 4.23–4.29 (m, 1 H), B 4.37–4.43 (m, 1 H), M 3.97 (m, 1 H), (DE) A 4.54–4.60 (m, 1 H), B 4.67–4.73 (m, 1 H), M 5.51 (m, 1 H), [3-(diethylamino)-1,2-propanediol] A 3.46–3.52 (m, 1 H), B + M 3.68–3.76 (m, 2 H).

Reactions of 3-(*N*-Benzyl-*N*-methylamino)-1,2-propanediol. (a) 3-(*N*-benzyl-*N*-methylamino)-1,2-propanediol (302 mg, 1.55 mmol) was reacted with dibutyltin oxide (408 mg, 1.64 mmol) and benzoyl chloride (218 mg, 1.55 mmol). After the reaction was quenched with trimethylsilyl chloride (337 mg, 3.10 mmol) according to method A, it was analyzed (Table II, entry 22) by ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABM part of an ABMXY system)): (mME) AB 3.75–3.86 (m, 2 H), M 5.37 (m, 1 H), (lME) A 4.20–4.26 (m, 1 H), B 4.38–4.50 (br m, 1 H), M 4.17 (br m, 1 H), (DE) A 4.47–4.53 (m, 1 H), B 4.64–4.70 (m, 1 H), M 5.62 (m, 1 H), (DS) AB + M 3.52–3.74 (br m, 3 H).

(b) 3-(*N*-Benzyl-*N*-methylamino)-1,2-propanediol (293 mg, 1.50 mmol) was reacted with dibutyltin oxide (392 mg, 1.58 mmol) and benzoyl chloride (211 mg, 1.50 mmol). The reaction was quenched with oxalic acid (68 mg, 0.76 mmol) according to method B, washed several times with a Na_2CO_3 saturated solution, then washed with water, and dried over anhydrous Na_2SO_4. After evaporation of the solvent, 475 mg of crude mixture was obtained and analyzed (Table II, entry 23) by ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABM part of an ABMXY system)): (mME) AB 3.88–3.99 (m, 2 H), M 5.27 (m, 1 H), (lME) A 4.22–4.28 (m, 1 H), B 4.39–4.45 (m, 1 H), M 4.10 (m, 1 H), (DE) A 4.50–4.56 (m, 1 H), B 4.65–4.70 (m, 1 H), M 5.63 (m, 1 H), [3-(*N*-benzyl-*N*-methylamino)-1,2-propanediol] A 3.45–3.51 (m, 1 H), B 3.67–3.73 (m, 1 H), M 3.83 (m, 1 H).

Reactions of 3-Methoxy-1,2-propanediol with Benzoyl Chloride. (a) 3-Methoxy-1,2-propanediol (107 mg, 1.01 mmol) was reacted with dibutyltin oxide (264 mg, 1.06 mmol) and benzoyl chloride (143 mg, 1.01 mmol). After the reaction was quenched with trimethylsilyl chloride (115 mg, 1.06 mmol) according to method A, it was analyzed (Table II, entry 24) by GC–MS and ^{1}H NMR: GC–MS (SE 30, 15 m; program 100 °C (3 min), 5 °C/min to 280 °C) (mME) t_R 14.14 min, MS (EI) m/z (relative intensity) 267 (3), 179 (23), 145 (11), 129 (10), 105 (100), 89 (16), 77 (32), 73 (20), 71 (16), 45 (14); (lME) t_R 14.44 min, MS (EI) m/z (relative intensity) 267 (2), 237 (23), 105 (100), 89 (10), 77 (20), 73 (21), 45 (11); ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(ROCH_2CHO)$ (R = PhCO, Me_3Si) (ABM part of an ABMXY system)) (mME) (mME) AB 3.66–3.68 (m, 2 H), M 5.25 (m, 1 H), (lME) A 4.24–4.32 (m, 1 H), B 4.36–4.42 (m, 1 H), M 4.13 (m, 1 H), (DE) AB 4.56–4.69 (m, 2 H), M 5.59 (m, 1 H), (DS) 3.40–3.70 (unresolved).

(b) 3-Methoxy-1,2-propanediol (159 mg, 1.50 mmol) was reacted with dibutyltin oxide (392 mg, 1.58 mmol) and benzoyl chloride (211 mg, 1.50 mmol). After the reaction was quenched with oxalic acid (68 mg, 0.75 mmol) according to method B, 340 mg of crude mixture was obtained and analyzed (Table II, entry 25) by ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(ROCH_2CHO)$ (R = PhCO, H) (ABM part of an ABMXY system)): (mME) AB 3.93–3.95 (br m, 2 H), M 5.26 (m, 1 H), (lME) AB 4.35–4.45 (m, 2 H), M 4.35 (br m, 1 H), (DE) AB 4.56–4.69 (m, 2 H), M 5.59 (m, 1 H), (3-methoxy-1,2-propanediol) AB 3.38–3.69 (unresolved), M 3.84 (m, 1 H).

Reactions of 4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane (Table III). (a) 2-Chlorobenzoyl Chloride. 4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane (185 mg, 0.50 mmol) was reacted in a 5-mm NMR tube with 2-chlorobenzoyl chloride (88 mg, 0.50 mmol) at room temperature for 15 min. After the reaction was quenched with trimethylsilyl chloride (57 mg, 0.53 mmol) according to method A, it was analyzed by ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABX)): (mME) A 3.86–3.91 (m, 1 H), B 3.96–4.03 (m, 1 H), X 6.09 (m, 1 H), (lME) A 4.38–4.45 (m, 1 H), B 4.54–4.59 (m, 1 H), X 5.06 (m, 1 H), (DE) AB 4.65–4.80 (m, 2 H), X 6.46 (m, 1 H), (DS) AB 3.57–3.68 (m, 2 H), X 4.73 (m, 1 H).

(b) 4-Methoxybenzoyl Chloride. 4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane (185 mg, 0.50 mmol) was reacted in a 5-mm NMR tube with 4-methoxybenzoyl chloride (85 mg, 0.50 mmol) at room temperature for 15 min. After the reaction was quenched with trimethylsilyl chloride (58 mg, 0.53 mmol) according to method A, it was analyzed by ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABX)): (mME) A 3.86–3.93 (m, 1 H), B 3.98–4.04 (m, 1 H), X 6.05 (m, 1 H), (lME) A 4.28–4.35 (m, 1 H), B 4.37–4.42 (m, 1 H), X 5.05 (m, 1 H), (DE) AB 4.59–4.74 (m, 2 H), X 6.38 (m, 1 H), (DS) AB 3.57–3.68 (m, 2 H), X 4.73 (m, 1 H).

(c) Acetyl Chloride. (1) 4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane (185 mg, 0.50 mmol) was reacted in a 5-mm NMR tube with acetyl chloride (39 mg, 0.50 mmol) at −25 °C for 10 min. After the reaction was quenched with trimethylsilyl chloride (57 mg, 0.52 mmol) according to method A, the reaction mixture was analyzed by ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABX)): (mME) AB 3.73–3.88 (m, 2 H), X 5.80 (m, 1 H), (lME) A 4.02–4.09 (m, 1 H), B 4.14–4.19 (m, 1 H), X 4.91 (m, 1 H), (DE) AB 4.25–4.37 (m, 2 H), X 6.01 (m, 1 H), (DS) AB 3.57–3.68 (m, 2 H), X 4.73 (m, 1 H).

(2) 4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane (185 mg, 0.50 mmol) was reacted in a 5-mm NMR tube with acetyl chloride (39 mg, 0.50 mmol) at −25 °C for 5 min. After the reaction was quenched with oxalic acid (23 mg, 0.26 mmol) for 2 h according to method B, 134 mg of crude mixture was obtained and analyzed by ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABX)): (mME) AB 3.75–3.88 (m, 2 H), X 5.82 (m, 1 H), (lME) A 4.11–4.18 (m, 1 H), B 4.23–4.28 (m, 1 H), X 4.94 (m, 1 H), (DE) AB 4.26–4.35 (m, 2 H), X 6.00 (m, 1 H), (1-phenyl-1,2-ethanediol) A 3.58–3.64 (m, 1 H), B 3.69–3.74 (m, 1 H), X 4.77 (m, 1 H). Separation by flash column chromatography, eluting with petroleum ether/ethyl acetate (50:50), gave 39 mg of mME in 43% yield, which isomerizes on standing.

1-Phenyl-1,2-ethanediol 1-*O*-acetyl ester: oil (regioisomeric mixture); GC (program 80 °C (4 min), 10 °C/min to 280 °C) t_R 10.10 (lME 11.10); MS (EI) m/z (relative intensity) 149 (7), 120 (35), 107 (100), 105 (14), 91 (10), 79 (71), 78 (12), 77 (42), 51 (18), 43 (93).

(d) Methoxyacetyl Chloride. 4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane (112 mg, 0.30 mmol) was reacted in a 5-mm NMR tube with methoxyacetyl chloride (32 mg, 0.30 mmol) at −78 °C for 5 min. After the reaction was quenched with trimethylsilyl chloride (34 mg, 0.32 mmol) according to method A, it was analyzed by ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABX)): (mME) AB 3.75–3.88 (m, 2 H), X 5.92 (m, 1 H), (lME) AB 4.19–4.33 (m, 2 H), X 4.91 (m, 1 H), (DE) AB 4.35–4.49 (m, 2 H), X 6.15 (m, 1 H), (DS) AB 3.57–3.68 (m, 2 H), X 4.73 (m, 1 H).

(e) Pivaloyl Chloride. 4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane (92 mg, 0.25 mmol) was reacted in a 5-mm NMR tube with pivaloyl chloride (30 mg, 0.25 mmol) at room temperature for 1 h. After the reaction was quenched with trimethylsilyl chloride (28 mg, 0.26 mmol) according to method A, it was analyzed by ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABX)): (mME) AB 3.66–3.81 (m, 2 H), X 5.76 (m, 1 H), (lME) AB 4.01–4.12 (m, 2 H), X 4.86 (m, 1 H), (DE) AB 4.19–4.32 (m, 2 H), X 5.98 (m, 1 H), (DS) AB 3.57–3.68 (m, 2 H), X 4.73 (m, 1 H).

(f) Acetic Anhydride. 4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane (210 mg, 0.57 mmol) was reacted in a 5-mm NMR tube

with acetic anhydride (58 mg, 0.57 mmol) at −60 °C for 10 min. After the reaction was quenched with oxalic acid (26 mg, 0.29 mmol) for 2 h according to method B, it was analyzed by ^{1}H NMR (300 MHz, $CDCl_3$, $\delta(OCH_2CHO)$ (ABX)): (mME) AB 3.73–3.87 (m, 2 H), X 5.82 (m, 1 H), (lME) A 4.10–4.17 (m, 1 H), B 4.22–4.27 (m, 1 H), X 4.92 (m, 1 H), (DE) AB 4.23–4.34 (m, 2 H), X 5.99 (m, 1 H), (1-phenyl-1,2-ethanediol) A 3.56–3.62 (m, 1 H), B 3.67–3.72 (m, 1 H), X 4.76 (m, 1 H).

The Liquid, Solid, and Molecular Force Field Calculated Conformations of Savinin

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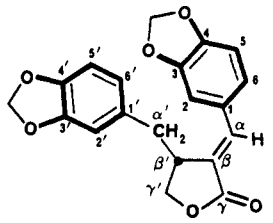
Following the unambiguous assignment of the ^{1}H and ^{13}C NMR spectra of the cytotoxic lignan savinin (1), its solution conformation has been studied through ^{1}H NMR spectroscopy. Surprisingly, evidence was found for overlap of the aromatic rings and for the proximate nature of H-2 and H-2′ and H-7 and H-7′. In contrast, the conformation in the solid state was established to be in a "spread-eagle" orientation, the energy of which was calculated to be 45.986 kcal/mol. Molecular force field calculations also gave evidence for two minima at 46.128 and 45.820 kcal/mol whose conformations were in agreement with the NOE data.

Introduction

The conformational analysis of small flexible molecules possessing biological activity is presently an area of great interest. Continuing our studies[2] in this area, we chose to examine the compound savinin (1), an α-arylidene γ-lactone lignan found in several plant species[3-10] and isolated by us as a cytotoxic constituent of *Aristolochia indica* roots.[11] The present study of savinin (1) was originally



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initiated to establish unambiguous proton and carbon-13 NMR assignments. The interesting results that emanated from the NMR analysis prompted us to pursue a more detailed study of savinin (1) comparing its respective solution, solid, and calculated energy-minimized conformations. In the course of this study, a broad combination of complimentary 1D and 2D NMR techniques, including the homonuclear shift correlation (COSY), two-dimensional nuclear Overhauser experiments (NOESY), and hetero-

Table I. ^{1}H NMR Assignments, ^{1}H T_1 Data, and Observed Spatial Assignments of Savinin (1)

proton	δ,[a] ppm	^{1}H T_1,[b] s	cross peaks obsd (δ, ppm)[c]	
α_{ax}-H	2.524	0.6	α'_{eq}H	(2.930)
			H-6′	(6.577)
α'_{ax}-H	2.930	0.5	α'_{ax}-H	(2.524)
			H-2	(6.982)
			H-2′	(6.609)
β′-H	3.680	0.9	γ'_{cis}-H	(4.204 or 4.187)
			H-2′	(6.609)
$\gamma'_{cis,trans}$-H	4.204 or 4.187	0.7	β′-H	(3.680)
			H-6′	(6.577)
α-H	7.431	2.6	H-6	(7.206)
H-6	7.206	1.4	H-5	(6.821)
			α-H	(7.431)
H-2	6.982	1.6	H-6′	(6.577)
H-5	6.821	2.8	H-6	(7.206)
OCH_2O[d]	5.985	1.4	H-2	(6.982)
			H-5	(6.821)
OCH_2O[e]	5.820, 5.881	1.5	H-2′	(6.609)
			H-5′	(6.675)
H-6′	6.577	1.8	H-5′	(6.675)
			H-2	(6.982)
			α'_{ax}-H	(2.574)
H-5′	6.675	2.7	H-6′	(6.577)
H-2′	6.609	2.3	β′-H	(3.680)
			H-2	(6.982)
			α'_{eq}-H	(2.930)

[a] All chemical shifts are expressed in parts per million relative to tetramethylsilane (TMS) δ = 0.00 ppm. [b] Measured by using an inversion-recovery sequence. Sample concentration = 40 mg/0.5 mL in $CDCl_3$ at 25 °C. The SD for the T_1 data is ±1–5%. [c] Determined from proton 2D NOE (NOESY) results (mixing time = 3.0 s). [d] Conjugated ring. [e] Saturated ring.

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