Masked Lithium Bishomoenolates: Useful Intermediates in Organic Synthesis

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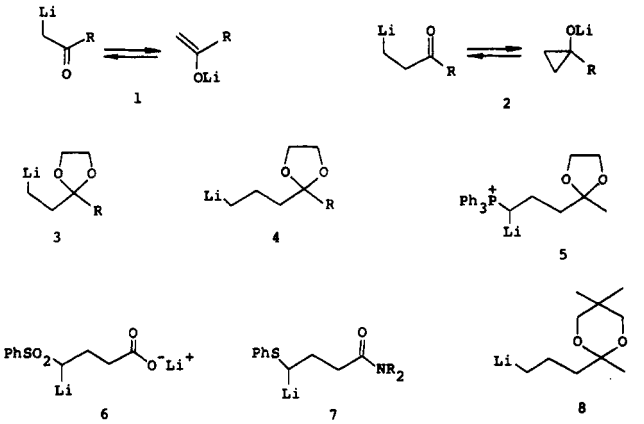
The lithiation of the chloro ketals **9** with lithium naphthalenide at -78 °C led to the corresponding masked lithium bishomoenolates **4**, which are stable species under these conditions and react with different electrophilic reagents (H_2O, D_2O, *i*-PrCHO, PhCHO, MeCOEt, $(CH_2)_4CO$, $(CH_2)_5CO$, $(CH_2)_7CO$, PhCOMe, c-C_3H_5COPh, PhCN, $HCONMe_2$, $PrCON(CH_2)_4$, $PhCON(CH_2)_4$, PhCOCl, EtOCOCl, PhCHNPh, and $(PhCH_2S)_2$) to give, after hydrolysis with water, the corresponding bifunctionalized compounds **10a-22a**, **10b-22b**, and **10c-15c**. When alkyl halides were used as electrophiles the reaction failed. In the presence of a catalytic amount of the complex $CuBr{\cdot}Me_2S$, the same reaction with α,β-unsaturated ketones (methyl vinyl ketone or 2-cyclohexanone) yielded the expected products of a 1,4-addition **25a-c** and **26b**. The deprotection of the masked carbonyl group was easily done by treatment with 2 N hydrochloric acid in THF, so as examples, compounds **27a-29a**, **30b**, **31b**, **32c**, and **33c** were isolated. The transformation of hemiacetals of the type **27a** into substituted tetrahydropyrans was carried out by means of compounds of the type R_3SiNu (Nu = H, allyl, CN) in the presence of BF_3, so products **34a-41a**, **42b**, and **43b** were prepared. Finally, the in situ oxidation of the deprotected products of the type **27a**—arising from the reaction of bishomoenolate **4a** with carbonyl compounds—with Jones reagent (for ketones derivatives) or PCC (for aldehydes derivatives) led to the corresponding δ-lactones **44-57**.

Introduction

The chemistry of functionalized organometallic compounds derived from metals of the main groups has been the subject of great attention because these intermediates can react with electrophiles, yielding directly polifunctionalized molecules.[1] In the case that the functionality is a carbonyl group and the metal atom is lithium,[2] the stability of these species depends strongly on the relative position of the metal atom and the carbon-oxygen double bond.[3] Thus, since enolate intermediates[4] of the type **1** are stable species, which give C-coupling reactions,[5] the corresponding homoenolate intermediates of the type **2** behave as typical alcoholates.[6] The problem of using homoenolate intermediates in organic synthesis, mainly in homoaldolic-type reactions, has been overcome by employing two different strategies: (a) forming more stable homoenolates derived from less electropositive metals, such as Ti, Sn, Sb, Bi, Te, Hg, or Zn,[7] or (b) protecting the carbonyl group as a ketal of the type **3**.[8] In relation to the corresponding lithium bishomoenolates of the type **4**,[9]

Chart I



in the literature are described stabilized species of the type **5**,[13] **6**,[14] and **7**.[15] To our best knowledge, only one example of a masked nonstabilized intermediate **8** is known,[16] which has been used in the synthesis of (±)-porantherine[17a] and substituted piperidines.[17b] This species must be prepared at low temperature, and its yield is quite sensitive to the reaction conditions[17a] (see Chart I). In this paper,[18] we describe the general preparation of different lithium masked bishomoenolates of the type **4**, which represent convenient synthons[19] for the unit C—C—C—C=O and can be considered as d^4 reagents, following Seebach's nomenclature.[20]

(1) See, for instance: (a) *Comprehensive Organic Chemistry*; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon Press: Oxford, 1979; Vol. 3, Part 15. (b) Negishi, E.-I. *Organometallics in Organic Synthesis*; J. Wiley & Sons: New York, 1980.

(2) (a) Wakefield, B. J. *Organolithium Methods*; Academic Press: London, 1988. (b) *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed.; George Thieme Verlag: Stuttgart, 1970; Vol. 13/1.

(3) *Umpoled Synthons*; Hase, T. A., Ed.; J. Wiley & Sons: New York, 1987.

(4) For an excellent review, see: Seebach, D. *Angew. Chem.* **1988**, *100*, 1685; *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624.

(5) See, for instance: Bates, R. B.; Ogle, C. A. *Carbanion Chemistry*; Springer Verlag: Berlin, 1983; Chapter V.

(6) (a) Werstiuk, N. H. *Tetrahedron* **1983**, *39*, 205. (b) Stowell, J. C. *Chem. Rev.* **1984**, *84*, 409. (c) Hoppe, D. *Angew. Chem.* **1984**, *96*, 930; *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 932.

(7) See, for instance: Nakamura, E.; Shimada, J.; Kuwajima, I. *Organometallics* **1985**, *4*, 641.

(8) (a) Barluenga, J.; Rubiera, C.; Fernández, J. R.; Yus, M. *J. Chem. Soc., Chem. Commun.* **1987**, 425. (b) Barluenga, J.; Fernández, J. R.; Yus, M. *Ibid.* **1987**, 1534. (c) Barluenga, J.; Fernández, J. R.; Rubiera, C.; Yus, M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3113.

(9) The corresponding bishomoenolates of other less electropositive metals such as magnesium,[10] copper,[11] or zinc[12] have been already described.

(10) (a) Bal, S. A.; Marfat, A.; Helquist, P. *J. Org. Chem.* **1982**, *47*, 5045. (b) Joshi, N. N.; Mandapur, V. R.; Chadha, M. S. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2963. (c) Achmatowicz, B.; Wicha, J. *Liebigs Ann. Chem.* **1988**, 1135.

(11) Wehmeyer, R. M.; Rieke, R. D. *Tetrahedron Lett.* **1988**, *29*, 4513.

(12) (a) Ochiai, H.; Nishihara, T.; Tamaru, Y.; Yoshida, Z. *J. Org. Chem.* **1988**, *53*, 1343. (b) Tamaru, Y.; Tanigawa, H.; Yamamoto, T.; Yoshida, Z. *Angew. Chem.* **1989**, *101*, 358; *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 353. (c) Tamaru, Y.; Ochiai, H.; Nakamura, T.; Yoshida, Z. *Org. Synth.* **1988**, *67*, 98.

(13) Camps, F.; Sanchez, F. J.; Messeguer, A. *Synthesis* **1988**, 823.

(14) Thomson, C. M.; Frick, J. A. *J. Org. Chem.* **1989**, *54*, 890, and references cited therein.

(15) Beak, P.; Hunter, J. E.; Jung, Y. M.; Wallin, A. P. *J. Am. Chem. Soc.* **1987**, *109*, 5403.

(16) In our preliminary communication,[18] we unintentionally omitted the citation of this sole example. We thank Dr. D. M. Ryckman for calling our attention to his previous publications,[17] in which this intermediate was involved.

(17) (a) Ryckman, D. M.; Stevens, R. V. *J. Am. Chem. Soc.* **1987**, *109*, 4940. (b) Ryckman, D. M.; Stevens, R. V. *J. Org. Chem.* **1987**, *52*, 4274.

(18) For preliminary communications, see: (a) Ramón, D. J.; Yus, M. *Tetrahedron Lett.* **1990**, *31*, 3763. (b) Ramón, D. J.; Yus, M. *Ibid.* **1990**, *31*, 3767.

(19) Corey, E. J. *Pure Appl. Chem.* **1967**, *14*, 19. See also ref 3.

0022-3263/91/1956-3825$02.50/0

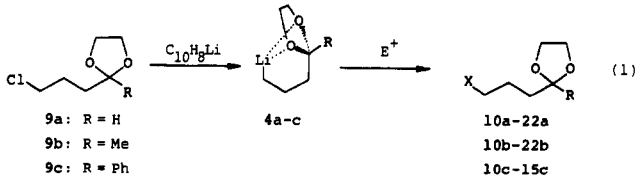
Table I. Reaction of Masked Bishomoenolates 4 with Electrophiles (eq 1)

entry	bishomoenolate 4	E^+	product[a] no.	X	yield[b] (%)
1	4a	H_2O	10a	H	85
2	4a	*i*-PrCHO	11a	*i*-PrCH(OH)	61
3	4a	PhCHO	12a	PhCH(OH)	60
4	4a	MeCOEt	13a	MeC(OH)Et	62
5	4a	$(CH_2)_4CO$	14a	$(CH_2)_4C(OH)$	67
6	4a	$(CH_2)_5CO$	15a	$(CH_2)_5C(OH)$	62
7	4a	$(CH_2)_7CO$	16a	$(CH_2)_7C(OH)$	60
8	4a	PhCOMe	17a	PhC(OH)Me	64
9	4a	c-C_3H_5COPh	18a	c-C_3H_5C(OH)Ph	57
10	4a	PhCN	19a	PhCO	56
11	4a	$PhCON(CH_2)_4$	19a	PhCO	57
12	4a	PhCOCl	19a	PhCO	36
13	4a	PhNCS	20a	PhNHCS	65
14	4a	PhCHNPh	21a	PhCH(PhNH)	61
15	4a	$(PhCH_2S)_2$	22a	$PhCH_2S$	85
16	4b	H_2O	10b	H	90
17	4b	D_2O	11b[c]	D	80
18	4b	*i*-PrCHO	12b	*i*-PrCH(OH)	52
19	4b	PhCHO	13b	PhCH(OH)	51
20	4b	$(CH_2)_5CO$	14b	$(CH_2)_5C(OH)$	61
21	4b	c-C_3H_5COPh	15b	c-C_3H_5C(OH)Ph	78
22	4b	PhCN	16b	PhCO	62
23	4b	$HCONMe_2$	17b	HCO	42
24	4b	$PrCON(CH_2)_4$	18b	PrCO	53
25	4b	$PhCON(CH_2)_4$	16b	PhCO	55
26	4b	PhCOCl	16b	PhCO	24
27	4b	EtOCOCl	19b	EtOCO	42
28	4b	PhNCS	20b	PhNHCS	73
29	4b	PhCHNPh	21b	PhCH(PhNH)	82
30	4b	$(PhCH_2S)_2$	22b	$PhCH_2S$	62
31	4c	PhCHO	10c	PhCH(OH)	75
32	4c	$(CH_2)_5CO$	11c	$(CH_2)_5C(OH)$	70
33	4c	c-C_3H_5COPh	12c	c-C_3H_5C(OH)Ph	49
34	4c	PhCN	13c	PhCO	55
35	4c	PhNCS	14c	PhNHCS	80
36	4c	$(PhCH_2S)_2$	15c	$PhCH_2S$	75

[a] All products were ≥95% pure (GLC and NMR). [b] Isolated yields after flash chromatography based on the starting material 9. [c] ≥95% deuterium from mass spectrometry.

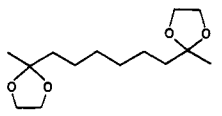
Results and Discussion

The reaction of the chloro ketals **9** with lithium naphthalenide[21,22] in THF at −78 °C led to the corresponding masked lithium bishomoenolates **4**, which were stable species at this temperature, and reacted with different electrophilic reagents (−78 °C to room temperature) to give, after hydrolysis, the expected products **10a–22a**, **10b–22b**, and **10c–15c** (see eq 1 and Table I). Dioxalanylpropyllithium reagents **4** have to be manipulated at low temperature in order to avoid their partial or total decomposition under the reaction conditions mainly by abstraction of a proton from the solvent.[22,23]



$E^+ = H_2O$, D_2O, *i*-PrCHO, PhCHO, MeCOEt, $(CH_2)_4CO$, $(CH_2)_5CO$, $(CH_2)_7CO$, PhCOMe, c-C_3H_5COPh, PhCN, $HCONMe_2$, $PrCON(CH_2)_4$, $PhCON(CH_2)_4$, PhCOCl, EtOCOCl, PhNCS, PhCHNPh, $(PhCH_2S)_2$

The reaction of lithium reagents **4** with alkyl chlorides or bromides failed. Thus, when the bishomoenolate **4b** was treated with 2-chloropropene or ethyl, isopropyl, or allyl bromide under the same conditions as in the previous text or even in the presence of a copper(I) salt (bromide or cyanide) or TMEDA only the corresponding product **10b**, arising from a proton abstraction from the reaction media, was isolated. On the other hand, when methyl iodide was used as electrophile, the corresponding Wurtz-type product **23** was isolated in 32% yield. Finally, the use of nitriles or anhydrides containing hydrogen atoms in the α position (acetonitrile or acetic anhydride) led also to a lithium–hydrogen interchange; in these cases, the acidity of the mentioned hydrogen atoms could explain this behavior.



23

We have also studied the reaction of organolithium reagents **4** with α,β-unsaturated ketones **24**, such as methyl vinyl ketone or 2-cyclohexenone, in the presence of a catalytic amount (1/0.25 molar ratio) of the complex copper(I) bromide–dimethyl sulfide[10a] under the same reaction conditions as in the previous text. Thus, the expected products **25** or **26** were isolated (eq 2 and Table II).

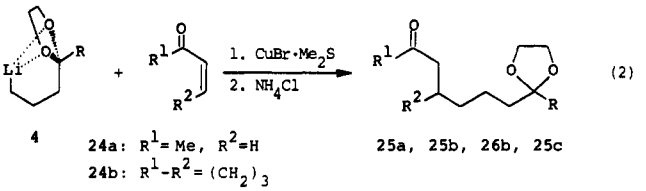


Table II. Reaction of Organolithium Reagents 4 with α,β-Unsaturated Ketones 24 Catalyzed by CuBr·Me_2S (eq 2)

entry	bishomoenolate 4	carbonyl compound 24	product[a] no.	R^1	R^2	yield[b] (%)
1	4a	24b	25a	$-(CH_2)_3-$		61
2	4b	24a	25b	Me	H	41
3	4b	24b	26b	$-(CH_2)_3-$		63
4	4c	24b	25c	$-(CH_2)_3-$		54

[a,b] See footnotes *a* and *b* in Table I.

From the results summarized in both Table I and II, we think that compounds **11–22**, **25**, and **26** are interesting from a synthetic point of view because they contain, in general, two functional groups, one of them (the masked carbonyl group arising from **4**) in a protected form, so they are regioselectively protected bifunctional compounds. The deprotection of these compounds can be carried out easily by acid hydrolysis (20 °C), yielding the corresponding functionalized carbonyl compounds in high yields. Thus, as examples, the treatment of compounds **17a**, **19a**, **22a**, **18b**, **26b**, **13c**, and **15c** with 2 N hydrochloric acid in THF afforded products **27a** (99%), **28a** (93%), **29a** (95%), **30b** (87%), **31b** (94%), **32c** (98%), and **33c** (99%), respectively (see Chart II). On the other hand, compounds

(20) Seebach, D. *Angew. Chem.* **1979**, *91*, 259; *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.
(21) The lithiation with lithium powder at −78 °C failed: Flórez, J. Ph. D. Thesis, University of Oviedo, 1984.
(22) (a) Barluenga, J.; Flórez, J.; Yus, M. *J. Chem. Soc., Chem. Commun.* **1982**, 1153. (b) Barluenga, J.; Flórez, J.; Yus, M. *J. Chem. Soc., Perkin Trans. 1* **1983**, 3019.
(23) (a) Bates, R. B.; Kroposki, L. M.; Potter, D. E. *J. Org. Chem.* **1972**, *37*, 560. (b) Mills, N. S.; Shapiro, J.; Hollingsworth, M. *J. Am. Chem. Soc.* **1981**, *103*, 1263.

Chart II

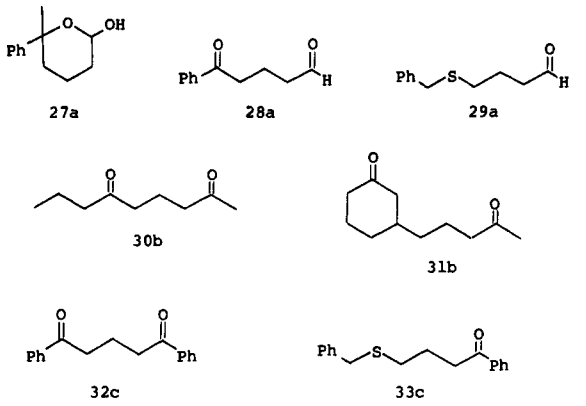


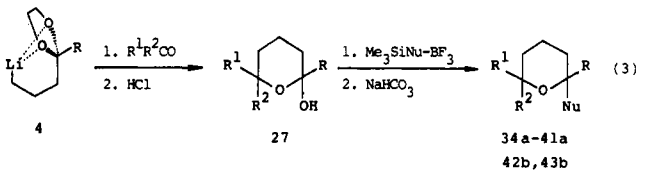
Table III. Preparation of Substituted Pyrans 34–43 (eq 3)

entry	bishomo-enolate 4	carbonyl compound R^1	carbonyl compound R^2	Nu	product[a] no.	product[a] yield[b] (%)
1	**4a**	$-(CH_2)_5-$		H[c]	**34a**	61
2	**4a**	Et	Et	CH_2=$CHCH_2$	**35a**	55
3	**4a**	$-(CH_2)_4-$		CH_2=$CHCH_2$	**36a**	47
4	**4a**	$-(CH_2)_5-$		CH_2=$CHCH_2$	**37a**	50
5	**4a**	Et	Et	CN	**38a**	62
6	**4a**	$-(CH_2)_4-$		CN	**39a**	41
7	**4a**	$-(CH_2)_5-$		CN	**40a**	47
8	**4a**	Ph	H	CN	**41a**[d]	53[d]
9	**4b**	$-(CH_2)_5-$		CH_2=$CHCH_2$	**42b**	40
10	**4b**	$-(CH_2)_5-$		CN	**43b**	38

[a,b] See footnotes *a* and *b* in Table I. [c] Et_3SiH was used instead of Me_3SiH. [d] A 43%/10% mixture of *trans*/*cis* diastereoisomers was obtained after isolation by flash chromatography.

of the type **31b** have been successfully employed in annulation reactions.[10a]

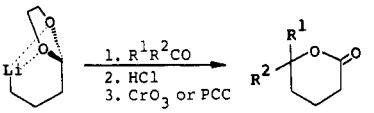
Compounds of the type **27a** can be used as precursors of substituted tetrahydropyrans.[24] Thus, by the use of silane derivatives it is possible to obtain the reduction,[25] allylation,[26] and introduction of a cyano group[27] in the tetrahydropyran ring. By this methodology, and starting from carbonyl compounds and the intermediates **4**, compounds **34a–41a**, **41b**, and **42b** were isolated (see eq 3 and



(3)

Table III). On the other hand, it is known[28] that there is the possibility of transforming compounds of the type **27a** into the corresponding alkylated ones by treatment of the 2,4-dimethoxybenzoyl derivatives with organocuprates.

Finally, we have studied the possibility of carrying out the oxidation of compounds of the type **27a** in order to obtain the corresponding δ-lactones.[29] We first studied the oxidation of compound **27a** with different reagents such as *m*-CPBA,[8c] MMPP,[30] PCC,[31] or Fetizon's reagent.[32] In all cases, surprisingly, the reaction failed, recovering the starting material. However, the use of Jones's reagent[33] worked very well giving the expected lactone **50** in 82% isolated yield[18b] (eq 4). We then applied this procedure,



(4)

44: R^1 = H, R^2 = i-Pr
45: R^1 = H, R^2 = n-C_5H_{11}
46: R^1 = R^2 = Me
47: R^1 = Me, R^2 = Et
48: R^1 = Me, R^2 = i-Bu
49: R^1 = Me, R^2 = t-Bu
50: R^1 = Me, R^2 = Ph
51: R^1 = R^2 = Et
52: R^1 = Et, R^2 = Ph
53: R^1 = n-Pr, R^2 = Ph
54: R^1 = R^2 = Ph
55: R^1-R^2 = $(CH_2)_4$
56: R^1-R^2 = $(CH_2)_5$
57: R^1-R^2 = $(CH_2)_7$

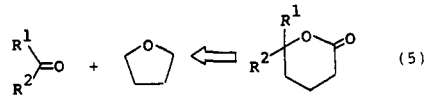
but carried out the reaction in situ, without isolation of the intermediates of the type **15a** or **27a**. Thus, the treatment of the intermediate **4a** with different ketones followed by hydrolysis with 2 N hydrochloric acid and final oxidation with the Jones's reagent gave the expected lactones **46–57** (33–62% overall yield;[18b] 28% for **54**; eq 4). When the same process was performed with aldehydes as electrophiles, the corresponding lactones were not isolated. Thus, for instance, with benzaldehyde the only reaction product isolated was 5-phenyl-5-oxopentanoic acid (35%), which arises from the total oxidation of both the secondary alcohol and the aldehyde functionalities. This problem was overcome (after trying the other previously mentioned oxidants) by using PCC[31] in the final step of the in situ method, so the corresponding δ-lactones **44** and **45** were isolated (eq 4). In some cases, mainly when the carbonyl compound is a phenone (products **50**, **52**, and **53**), the low overall yields obtained can be explained due to the competition of an enolization process, which leads to 2-propyl-1,3-dioxolane **10a** instead of the corresponding compound of the type **15a**.

Conclusions

From the results described in this paper, we conclude that intermediates of the type **4** are useful synthons for the unit C—C—C—C=O that can be adequate for the synthesis of biologically active compounds of the brevicomins type.[34] On the other hand, and considering the products prepared with anions **4**, we find especially interesting the compounds derived from aldehydes because there are important biologically active substances having

(24) Tetrahydropyrans are common structural elements in many biologically active natural products. See, for instance: Buchanan, J. G. *Prog. Chem. Nat. Org. Prod.* **1983**, *44*, 234.
(25) Kraus, G. A.; Frazier, K. A.; Roth, B. D.; Taschner, M. J.; Neuenschwander, K. *J. Org. Chem.* **1981**, *46*, 2417.
(26) Schmitt, A.; Reissig, H.-U. *Synlett.* **1990**, *1*, 40 and references cited therein.
(27) See, for instance: (a) Murakami, M.; Kato, T.; Mukaiyama, T. *Chem. Lett.* **1987**, 1167. (b) Kazmi, S. N.-ul-H.; Ahmed, Z.; Khan, A. Q.; Malik, A. *Synth. Commun.* **1988**, *18*, 151.
(28) Bolitt, V.; Mioskowski, C.; Falck, J. R. *Tetrahedron Lett.* **1989**, *30*, 6027.
(29) Lactonic functionality is fairly common among natural products and in a variety of biologically active molecules, the corresponding δ-lactones occurring preferentially in products from animal origin. See, for instance: Ohloff, G. *Prog. Chem. Nat. Org. Prod.* **1978**, *35*, 431.
(30) Brougham, P.; Cooper, N. S.; Cummerson, O. A.; Heany, H.; Thompson, N. *Synthesis* **1987**, 1015.
(31) Fujisawa, T.; Itoh, T.; Nakai, M.; Sato, T. *Tetrahedron Lett.* **1987**, *28*, 1015.
(32) Loozen, H. J. J.; Godefroi, E. F.; Bester, J. S. M. M. *J. Org. Chem.* **1975**, *40*, 892.
(33) Canonne, P.; Foscolos, G. B.; Belanger, O. *J. Org. Chem.* **1980**, *45*, 1828.
(34) See, for instance: (a) Ref. 10b. (b) Chong, J. M.; Mar, E. K. *Tetrahedron* **1989**, *45*, 7709.

this skeleton.[35] Thus, for instance, compound **45** is a constituent of massory bark (*Cryptocarya massoica*).[36] Moreover, spirolactones of the type **55–57** are also key structural features of many natural products,[37] and, in general, δ-lactones[29] are interesting materials for other types of functionalities.[25,38] Finally, if one considers that starting material **9a** is easily available from tetrahydrofuran (tandem opening with hydrogen chloride followed by PCC oxidation and final ketalization), the whole synthetic operation for **44–57** is that shown in eq 5.



(5)

Experimental Section

General Methods. Melting points are uncorrected. Flash column chromatography was done on Merck grade 60 silica gel (230–400 mesh), and TLC analyses were carried out on aluminum-backed plates coated with a 0.2-cm layer of silica gel 60H with a mixture of hexane/ethyl acetate as eluant (rates are given in each case); R_f values are given under these conditions (visualization by UV or/and vanillin). IR spectra were as films, unless otherwise stated. ^{1}H NMR spectra were obtained at 60 MHz in CCl_4 or at 300 MHz in $CDCl_3$. ^{13}C NMR spectra were obtained at 75 MHz in $CDCl_3$. Mass spectra (MS) were obtained at 70 eV. Microanalyses have been done for selected new compounds; for other new compounds the level of purity is indicated by the inclusion of copies of ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra as supplementary material. The purity of all isolated compounds (≥95%) was determined by GLC with the following: (a) a 25-m WCOT capillary column (0.22-mm diameter, 2.2-μm film thickness OV-101 stationary phase), $T_{injector}$ = 270 °C, T_{column} = 80 °C (3 min) and 80–270 °C (15 °C/min) (A conditions); (b) a 12-m HP-1 capillary column (0.20-mm diameter, 0.33-μm film thickness OV-1 stationary phase), $T_{injector}$ = 270 °C, T_{column} = 60 °C (3 min) and 60–270 °C (15 °C/min) (B conditions); (c) the same column as for b but $T_{injector}$ = 270 °C, T_{column} = 150 °C (3 min) and 150–270 °C (15 °C/min) (C conditions). N_2 (2 mL/min) was used as the carrier gas in all cases. Retention times (t_r) are given under these three conditions.

Electrophiles and other reagents were commercially available (Aldrich, Fluka, Merck) of the best grade and were used without further purification. Propanoylpyrrolidine,[39] benzoylpyrrolidine,[39] benzylideneaniline,[40] and lithium naphthalenide[41] were prepared according to the literature methods. Starting materials **4a** and **4b** were commercially available (Fluka), and **4c** was prepared according to the described method.[42] Tetrahydrofuran (THF) was dried successively with Na and $LiAlH_4$ under reflux and stored under Ar. Reactions that involved organolithium derivatives were carried out under Ar with use of oven-dried glassware.

Preparation of Bishomoenolates 4 and Reaction with Electrophiles. Isolation of Products 10–23, 25, and 26. General Procedure. To a solution of the corresponding dioxolane **9** (2.5 mmol) in THF (5 mL) was added a solution of lithium naphthalenide (6.0 mmol) in THF at −78 °C under Ar, and the mixture was stirred for 7 h at the same temperature. Then, the corresponding electrophile (2.5 mmol)[43] was added and the resulting solution was stirred overnight, allowing the temperature to rise to 20 °C. Then, the resulting mixture was hydrolyzed with water (5 mL), neutralized with 2 N HCl, and extracted with ether (2 × 5 mL) and the organic layer dried (Na_2SO_4). Solvents were removed in vacuo (15 Torr), and the resulting residue was chromatographed (silica gel; hexane/ethyl acetate) to give the corresponding products **10a–22a**, **10b–22b**, **10c–15c**, and **23**. In the case of using α,β-unsaturated ketones **24** as electrophiles, CuBr·Me_2S complex (0.6 mmol) was added after formation of the intermediates **4** and the mixture stirred for 30 min before adding the electrophile **24** (2.5 mmol); in these cases and final hydrolysis was carried out with a saturated aqueous NH_4Cl. Yields are reported in Tables I and II. Physical, spectral, and analytical data follow. Full spectral data for the known compounds **10a**,[44] **12a**,[45] **17a**,[47] **10b**,[48] **13b**,[46] **16b**,[49] **17b**,[50] **19b**,[51] and **25**[10a] are given as supplementary material.

2-(4-Hydroxy-5-methylhexyl)-1,3-dioxolane (11a): t_r = 11.87 min (B), R_f = 0.43 (3/2); IR 3420 (OH), 1250, 1030 (CO) cm^{-1}; ^{1}H NMR (60 MHz) δ 0.85 (d, J = 7, 6 H, 2 CH_3), 1.2–1.7 (m, 6 H, $(CH_2)_3$), 3.0–3.4 (m, 3 H, CHCHOH), 3.6–3.8 (m, 4 H, OCH_2CH_2O), 4.7 (t, J = 5, 1 H, OCHO); MS 187 (M^+ − 1, 1), 101 (12), 99 (12), 73 (100), 45 (91), 43 (86). Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.80; H, 10.70. Found: C, 64.0; H, 10.7.

2-(4-Hydroxy-4-methylhexyl)-1,3-dioxolane (13a): t_r = 10.32 min (B), R_f = 0.38 (3/2); IR 3440 (OH), 1130, 1030 (CO) cm^{-1}; ^{1}H NMR (60 MHz) δ 0.75–1.0 (m, 3 H, CH_3CH_2), 1.05 (s, 3 H, CH_3C), 1.15–1.7 (m, 9 H, $CH_2C(OH)(CH_2)_3$), 3.6–3.9 (m, 4 H, OCH_2CH_2O), 4.7 (t, J = 5, 1 H, CH); MS 188 (M^+, <1), 159 (29), 101 (34), 73 (100), 45 (83), 43 (81). Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.80; H, 10.70. Found: C, 63.45; H, 10.5.

2-[3-(1-Hydroxycyclopentyl)propyl]-1,3-dioxolane (14a): t_r = 11.85 min (B), R_f = 0.32 (3/2); IR 3400 (OH), 1120, 1010 (CO) cm^{-1}; ^{1}H NMR (60 MHz) δ 1.3–1.9 (m, 15 H, $(CH_2)_4C(OH)(CH_2)_3$), 3.6–3.9 (m, 4 H, OCH_2CH_2O), 3.7 (t, J = 5, 1 H, CH); MS 200 (M^+, <1), 138 (14), 99 (21), 88 (27), 73 (100), 45 (59). Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.95; H, 10.06. Found: C, 65.9; H, 9.7.

2-[3-(1-Hydroxycyclohexyl)propyl]-1,3-dioxolane (15a):[46] t_r = 13.74 min (A), R_f = 0.42 (3/2); IR 3420 (OH), 1120, 1020 (CO) cm^{-1}; ^{1}H NMR (60 MHz) δ 1.1–1.7 (m, 16 H, $(CH_2)_5C(CH_2)_3$), 2.15 (s, 1 H, OH), 3.6–3.8 (m, 4 H, OCH_2CH_2O), 4.7 (t, J = 5, 1 H, CH); MS 213 (M^+ − 1, 1), 153 (23), 101 (31), 73 (100), 45 (38).

2-[3-(1-Hydroxycyclooctyl)propyl]-1,3-dioxolane (16a): t_r = 14.91 min (B), R_f = 0.30 (3/2); IR 3440 (OH), 1130, 1020 (CO) cm^{-1}; ^{1}H NMR (60 MHz) δ 1.1–1.9 (m, 21 H, $(CH_2)_7C(OH)(CH_2)_3$), 3.6–3.85 (m, 4 H, OCH_2CH_2O), 3.65 (t, J = 5, 1 H, CH); MS 242 (M^+, <1), 181 (30), 127 (100), 101 (82), 96 (46), 63 (62). Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.0; H, 10.9.

2-(4-Cyclopropyl-4-hydroxy-4-phenylbutyl)-1,3-dioxolane (18a): t_r = 17.05 min (A), R_f = 0.61 (3/2); IR 3460 (OH), 3010, 1600, 1480 (Ph), 1200, 1030 (CO) cm^{-1}; ^{1}H NMR (60 MHz) δ 0.35 (t, J = 7, 4 H, 2 cyclopropyl CH_2), 1.05–1.6 (m, 6 H, $CHC(OH)CH_2(CH_2)_2$), 1.85 (t, J = 7, 2 H, CH_2COH), 3.6–3.9 (m, 4 H, OCH_2CH_2O), 4.6 (t, J = 5, 1 H, OCHO), 7.0–7.5 (m, 5 H, Ph); MS 262 (M^+, <1), 148 (11), 147 (100), 105 (63), 73 (38). Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.2; H, 8.4.

2-(3-Benzoylpropyl)-1,3-dioxolane (19a): t_r = 14.76 min (A), R_f = 0.43 (4/1); mp 77 °C (hexane/ether); IR (melted) 3040, 1590 (Ph), 1660 (C=O), 1240, 1020 (CO) cm^{-1}; ^{1}H NMR (60 MHz) δ 1.6–1.9 (m, 4 H, CH_2CH_2CH), 3.0 (t, J = 7, 2 H, CH_2C=O), 3.6–4.0 (m, 4 H, OCH_2CH_2O), 4.8 (t, J = 5, 1 H, OCHO), 7.3–7.6, 7.8–8.1 (2 m, 5 H, Ph); MS 220 (M^+, 4), 105 (66), 77 (100), 73 (50), 45 (35). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.2; H, 7.5.

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2-[3-[(Phenylamino)thiocarbonyl]propyl]-1,3-dioxolane (20a): t_r = 20.56 min (A), R_f = 0.41 (3/2); IR 3460, 3250, 1580 (NH), 3040, 1600 (Ph), 1380, 1140 (C=S), 1210, 1050 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 1.5–2.1 (m, 4 H, CH_2CH_2CH), 2.7 (t, J = 7, 2 H, CH_2CS), 3.6–3.95 (m, 4 H, OCH_2CH_2O), 4.75 (t, J = 5, 1 H, OCHO), 6.9–7.8 (m, 5 H, Ph), 9.5 (br s, 1 H, NH); MS 251 (M^+, 9), 218 (100), 147 (38), 99 (38), 77 (53), 73 (37). Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.82; N, 5.57. Found: C, 62.4; H, 6.8; N, 5.2.

2-[4-Phenyl-4-(phenylamino)butyl]-1,3-dioxolane (21a): t_r = 23.65 min (A), R_f = 0.43 (4/1); IR 3390, 1590 (NH), 3020, 1490 (Ph), 1250, 1030 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 1.4–1.95 (m, 6 H, $(CH_2)_3$), 3.6–4.0 (m, 5 H, OCH_2CH_2O, NH), 4.2 (t, J = 7, 1 H, CHN), 4.7 (t, J = 5, 1 H, OCHO), 6.15–6.35, 6.4–6.6, 6.7–7.05 (3 m, 5 H, PhN), 7.1–7.3 (m, 5 H, PhC); MS 297 (M^+, 5), 183 (12), 182 (100), 104 (15), 77 (12), 73 (10). Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.74; H, 7.79; N, 4.70. Found: C, 77.1; H, 8.0; N, 4.7.

2-[3-(Benzylthio)propyl]-1,3-dioxolane (22a): t_r = 15.71 min (A), R_f = 0.58 (4/1); IR 3010, 1590 (Ph), 1130, 1030 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 1.5–1.8 (m, 4 H, CH_2CH_2CH), 2.4 (t, J = 7, 2 H, SCH_2CH_2), 3.65 (s, 2 H, CH_2Ph), 3.7–3.9 (m, 4 H, OCH_2CH_2O), 4.7 (t, J = 1 H, OCHO), 7.3 (s, 5 H, Ph); MS 238 (M^+, 3), 147 (67), 91 (100), 73 (14), 45 (30). Anal. Calcd for $C_{13}H_{18}O_2S$: C, 65.51; H, 7.61. Found: C, 65.8; H, 7.9.

2-(3-Deuteriopropyl)-2-methyl-1,3-dioxolane (11b): t_r = 5.03 min (A), R_f = 0.69 (4/1); MS 131 (M^+, <1), 116 (19), 115 (12), 87 (100), 85 (14), 43 (51).

2-(4-Hydroxy-5-methylhexyl)-2-methyl-1,3-dioxolane (12b): t_r = 17.40 min (A), R_f = 0.60 (3/2); IR 3420 (OH), 1230, 1050 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 0.9 (d, J = 7, 6 H, $(CH_3)_2CH$), 1.25 (s, 3 H, CH_3C), 1.3–1.7 (m, 6 H, $(CH_2)_3$), 3.0–3.4 (m, 2 H, CHCH), 3.5 (s, 1 H, OH), 3.8 (s, 4 H, OCH_2CH_2O); MS 187 (M^+ - 15, 3), 97 (10), 87 (100), 55 (10), 43 (34). Anal. Calcd for $C_{11}H_{22}O_3$: C, 65.31; H, 10.96. Found: C, 65.6; H, 10.9.

2-[3-(1-Hydroxycyclohexyl)propyl]-2-methyl-1,3-dioxolane (14b):[46] t_r = 23.59 min (A), R_f = 0.23 (3/2); IR 3440 (OH), 1240, 1050 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 1.25 (s, 3 H, CH_3), 1.45 (m, 14 H, $\overline{(CH_2)_5C(CH_2)_2}$), 1.85 (s, 1 H, OH), 2.25 (m, 2 H, CH_2CO_2), 3.8 (s, 4 H, OCH_2CH_2O); MS 228 (M^+, <1), 115 (26), 99 (33), 87 (100), 71 (22), 43 (39).

2-(4-Cyclopropyl-4-hydroxy-4-phenylbutyl)-2-methyl-1,3-dioxolane (15b): t_r = 17.18 min (A), R_f = 0.33 (4/1); IR 3460 (OH), 3010, 1600 (Ph), 1220, 1065 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 0.35 (t, J = 6, 4 H, 2 cyclopropyl CH_2), 1.15 (s, 3 H, CH_3), 1.25–1.6 (m, 5 H, $CHCCH_2CH_2$), 1.8 (m, 2 H, CH_2CO_2), 2.0 (s, 1 H, OH), 3.75 (s, 4 H, OCH_2CH_2O), 7.0–7.5 (m, 5 H, Ph); MS 276 (M^+, 2), 147 (93), 115 (32), 105 (100), 87 (97), 43 (43). Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 73.9; H, 8.4.

2-Methyl-2-(4-oxoheptyl)-1,3-dioxolane (18b): t_r = 11.57 min (A), R_f = 0.47 (4/1); IR 1700 (C=O), 1200, 1060 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 0.9 (t, J = 7, 3 H, CH_3CH_2), 1.25 (s, 3 H, CH_3C), 1.45–1.8 (m, 6 H, CH_3CH_2, $CH_2CH_2CO_2$), 2.15–2.50 (m, 4 H, 2 CH_2C=O), 3.85 (s, 4 H, OCH_2CH_2O); MS 185 (M^+ - 15, 2), 99 (15), 87 (100), 43 (54), 41 (10). Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.06. Found: C, 65.6; H, 10.0.

2-[3-[(Phenylamino)thiocarbonyl]propyl]-2-methyl-1,3-dioxolane (20b): t_r = 20.67 min (A), R_f = 0.22 (4/1); IR 3460, 3250, 1580 (NH), 3040, 1600 (Ph), 1380, 1140 (C=S), 1210, 1050 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 1.35 (s, 3 H, CH_3), 1.6–2.1 (m, 4 H, $CH_2CH_2CO_2$), 2.9 (t, J = 7, 2 H, CH_2C=S), 7.0–7.8 (m, 5 H, Ph), 9.25 (br s, 1 H, NH); MS 265 (M^+, 20), 220 (68), 130 (74), 87 (76), 77 (68), 43 (100). Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.22; N, 5.28. Found: C, 63.2; H, 7.2; N, 5.6.

2-[4-Phenyl-4-(phenylamino)butyl]-2-methyl-1,3-dioxolane (21b): t_r = 39.09 min (A), R_f = 0.52 (4/1); IR 3380, 1580 (NH), 3020, 1600 (Ph), 1210, 1060 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.35 (s, 3 H, CH_3), 1.52–1.95 (m, 7 H, $(CH_2)_3$, NH), 3.90–4.00 (m, 4 H, OCH_2CH_2O), 4.50 (t, J = 6.7, 1 H, CHN), 6.55–6.60, 6.65–6.75, 7.10–7.20 (3 m, 5 H, PhN), 7.35–7.45 (m, 5 H, PhC); MS 311 (M^+, 7), 183 (14), 182 (100), 117 (13), 104 (22), 87 (19), 77 (29). Anal. Calcd for $C_{20}H_{25}NO_2$: C, 77.14; H, 8.09; N, 7.50. Found: C, 76.8; H, 8.3; N, 7.3.

2-[3-(Benzylthio)propyl]-2-methyl-1,3-dioxolane (22b): t_r = 15.77 min (A), R_f = 0.67 (4/1); IR 3020, 1595 (Ph), 1210, 1050 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 1.2 (s, 3 H, CH_3), 1.5–1.8 (m, 4 H, $CH_2CH_2CO_2$), 2.3 (t, J = 6, 2 H, CH_2CH_2S), 3.55 (s, 2 H, CH_2Ph), 3.75 (s, 4 H, OCH_2CH_2O), 7.1 (s, 5 H, Ph); MS 252 (M^+, 18), 161 (76), 115 (65), 99 (68), 91 (100), 87 (100), 43 (63). Anal. Calcd for $C_{14}H_{20}O_2S$: C, 66.63; H, 7.99. Found: C, 66.7; H, 8.1.

2-(4-Hydroxy-4-phenylbutyl)-2-phenyl-1,3-dioxolane (10c): t_r = 11.58 min (C), R_f = 0.39 (4/1); IR 3400 (OH), 3020, 1600 (Ph), 1170, 1030 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.15–1.85 (m, 6 H, $(CH_2)_3$), 2.72 (s, 1 H, OH), 3.35–3.85 (m, 4 H, OCH_2CH_2O), 4.35–4.45 (m, 1 H, CHO), 6.90–7.40 (m, 10 H, 2 Ph); ^{13}C NMR δ 19.8, 38.9, 39.9, 64.15, 64.2, 110.2, 125.5, 125.6, 127.05, 127.55, 127.85, 128.1, 142.3, 144.8; MS 254 (M^+ - 44, <1), 149 (100), 105 (54), 79 (17), 77 (45).

2-[3-(1-Hydroxycyclohexyl)propyl]-2-phenyl-1,3-dioxolane (11c): t_r = 10.63 min (C), R_f = 0.48 (4/1); IR 3400 (OH), 3040, 1600 (Ph), 1070, 1040 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.20–1.95 (m, 17 H, $\overline{(CH_2)_5C(OH)(CH_2)_3}$), 3.70–4.00 (m, 4 H, OCH_2CH_2O), 7.20–7.50 (m, 5 H, Ph); ^{13}C NMR δ 16.95, 22.1, 25.75, 34.8, 37.25, 40.9, 63.55, 64.35, 110.4, 124.4, 125.6, 127.95, 142.55; MS 290 (M^+, <1), 150 (10), 149 (100), 105 (51), 77 (27), 55 (11).

2-(4-Cyclopropyl-4-hydroxy-4-phenylbutyl)-2-phenyl-1,3-dioxolane (12c): t_r = 13.01 min (C), R_f = 0.54 (4/1); IR 3460 (OH), 3040, 1590 (Ph), 1170, 1030 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 0.20–0.50 (m, 4 H, 2 cyclopropyl CH_2), 1.15–1.45 (m, 3 H, CHCO, $CH_2CH_2CO_2$), 1.59 (s, 1 H, OH), 1.70–2.00 (m, 4 H, $CH_2CH_2CH_2$), 3.60–4.00 (m, 4 H, OCH_2CH_2O), 7.10–7.45 (m, 10 H, 2 Ph); ^{13}C NMR δ 0.55, 1.4, 21.8, 40.4, 42.25, 84.35, 84.4, 110.45, 125.5, 125.65, 126.45, 127.7, 127.9, 128.0, 142.6, 146.5; MS 193 (M^+ - 145, 1), 149 (83), 147 (24), 105 (100), 77 (54).

2-(3-Benzoylpropyl)-2-phenyl-1,3-dioxolane (13c): t_r = 11.82 min (C), R_f = 0.71 (4/1); IR 3040, 1580 (Ph); 1660 (C=O), 1180, 1030 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.65–1.74 (m, 2 H, CH_2CH_2C=O), 1.84–1.89 (m, 2 H, CH_2CO_2), 2.79 (t, J = 7.3, 2 H, CH_2C=O), 3.57–3.86 (m, 4 H, OCH_2CH_2O), 7.15–7.84 (m, 10 H, 2 Ph); ^{13}C NMR δ 18.2, 38.1, 39.5, 64.2, 110.0, 125.5, 127.6, 127.8, 127.9, 128.3, 128.4, 134.6, 136.8, 199.7; MS 296 (M^+, <1), 150 (10), 149 (100), 105 (65), 77 (52).

2-Phenyl-2-[3-[(phenylamino)thiocarbonyl]propyl]-1,3-dioxolane (14c): t_r = 16.29 min (C), R_f = 0.37 (4/1); IR 3240 (NH), 3040, 1540 (Ph), 1380, 1140 (C=S), 1210, 1040 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.75–2.10 (m, 4 H, $CH_2CH_2CO_2$); 2.8 (t, J = 7.05, 2 H, CH_2C=S), 3.65–4.10 (m, 4 H, OCH_2CH_2O), 7.15–1.80 (m, 10 H, 2 Ph), 9.40 (br s, 1 H, NH); ^{13}C NMR δ 23.3, 37.95, 43.3, 64.0, 110.1, 123.35, 125.25, 126.25, 127.65, 127.85, 128.35, 138.5, 141.75, 204.25; MS 327 (M^+, 7), 282 (37), 178 (47), 149 (80), 105 (94), 77 (100).

2-[3-(Benzylthio)propyl]-2-phenyl-1,3-dioxolane (15c): t_r = 12.46 min (C), R_f = 0.82 (4/1); IR 3040, 1580 (Ph), 1180, 1030 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.55–1.70 (m, 2 H, CH_2CH_2S), 1.90–2.00 (m, 2 H, CH_2CO_2), 2.35 (t, J = 7.35, 2 H, CH_2CH_2S), 3.59 (s, 2 H, CH_2Ph), 3.63–4.0 (m, 4 H, OCH_2CH_2O), 7.20–7.41 (m, 10 H, 2 Ph); ^{13}C NMR δ 23.1, 31.0, 35.7, 39.2, 64.3, 109.9, 125.5, 126.6, 127.9, 128.3, 128.6, 128.7, 138.3, 142.3; MS 314 (M^+, 3), 149 (100), 121 (20), 105 (57), 91 (59), 77 (30), 65 (12). Anal. Calcd for $C_{19}H_{22}O_2S$: C, 72.57; H, 7.05. Found: C, 72.9; H, 7.2.

2,9-Bis(ethylenedioxy)decane (23): t_r = 7.10 min (A), R_f = 0.57 (4/1); IR 1220, 1040 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 1.25 (s, 6 H, 2 CH_3), 1.5–2.2 (m, 8 H, $(CH_2)_4CH_2CO_2$), 3.0–3.3 (m, 4 H, 2 CH_2CO_2), 3.85 (s, 8 H, 2 OCH_2CH_2O); MS 243 (M^+ - 15, <1), 241 (12), 87 (100), 43 (44). Anal. Calcd for $C_{14}H_{26}O_4$: C, 65.09; H, 10.14. Found: C, 64.7; H, 10.1.

2-Methyl-2-(6-oxoheptyl)-1,3-dioxolane (25b): t_r = 11.94 min (A), R_f = 0.36 (4/1); IR 1700 (C=O), 1210, 1060 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 1.2 (s, 3 H, CH_3CO_2), 1.3–1.7 (m, 8 H, $(CH_2)_4CO_2$), 2.05 (s, 3 H, CH_3CO), 2.35 (t, J = 7, 2 H, CH_2CO), 3.75 (s, 4 H, OCH_2CH_2O); MS 185 (M^+ - 15, 6), 87 (43), 55 (11), 43 (100), 42 (10), 41 (10). Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.06. Found: C, 66.0; H, 9.8.

2-Methyl-2-[3-(3-oxocyclohexyl)propyl]-1,3-dioxolane (26b): t_r = 14.30 min (B), R_f = 0.55 (3/2); IR 1690 (C=O), 1220, 1050 (CO) cm^{-1}; ^1H NMR (60 MHz) δ 1.25 (s, 3 H, CH_3), 1.3–2.4 (m, 15 H, $\overline{CH_2CO(CH_2)_3CH(CH_2)_3}$), 3.8 (s, 4 H, OCH_2CH_2O); MS 211 (M^+ - 15, 2), 87 (100), 55 (10), 43 (38), 41 (14). Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.9; H, 9.9.

2-[3-(3-Oxocyclohexyl)propyl]-2-phenyl-1,3-dioxolane (25c): t_r = 10.99 min (C), R_f = 0.50 (4/1); IR 3040, 1600 (Ph),

1695 (C=O), 1180, 1030 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.15–2.65 (m, 15 H, $CH_2CO(CH_2)_3CH(CH_2)_3$), 3.65–4.20 (m, 4 H, OCH_2CH_2O), 7.00–7.70 (m, 5 H, Ph); ^{13}C NMR δ 20.75, 25.25, 31.25, 36.6, 39.05, 40.5, 41.45, 48.1, 64.45, 110.3, 125.7, 127.8, 128.0, 142.5, 206.75; MS 288 (M^+ – 77, <1), 149 (100), 105 (40), 77 (23), 55 (10).

Deprotection of Dioxolanes 17a, 19a, 22a, 18b, 26b, and 15c. Isolation of Compounds 27a–29a, 30b, 31b, 32c, and 33c. General Procedure. The corresponding dioxolane (2 mmol) was dissolved in THF (5 mL) and 2 N HCl (5 mL) and the solution stirred for 2 h at room temperature. Then, it was extracted with ether (2 × 10 mL) and the organic layer dried (Na_2SO_4). Solvents were removed in vacuo (15 Torr), giving a residue, which contained pure title compounds. Yields are given in the text. Physical, spectral, and analytical data follow.

2-Methyl-2-phenyltetrahydrofuran-6-ol (27a):[52] t_r = 11.97 min (A), R_f = 0.55 (4/1); IR 3400 (OH), 3040, 1580 (Ph), 1060, 1010 (CO) cm^{-1}; ^1H NMR (60 MHz), δ 1.0–2.3 (m, 9 H, $(CH_2)_3$, CH_3), 3.3–3.9 (m, 2 H, CHOH), 6.8–7.3 (m, 5 H, Ph); MS 174 (M^+ – 18, 11), 118 (100), 117 (84), 115 (46), 103 (46), 77 (62).

4-Benzoylbutanal (28a):[53] t_r = 12.70 min (A), R_f = 0.35 (4/1); mp 117 °C (hexane/ether); IR (melted) 3040, 1590 (Ph), 2700, 1705 (HC=O), 1660 (C=O) cm^{-1}; ^1H NMR (60 MHz) δ 1.6–2.2 (m, 2 H, CH_2CH_2CO), 2.3–2.7 (m, 2 H, CH_2CHO), 2.95 (t, J = 7, 2 H, CH_2COPh), 7.3–7.6, 7.8–8.0 (2 m, 5 H, Ph), 9.75 (t, J = 1.5, 1 H, CHO); MS 171 (M^+ – 1, 7), 147 (10), 105 (100), 77 (99), 51 (38), 42 (43).

4-(Benzylthio)butanal (29a): t_r = 13.56 min (A), R_f = 0.53 (4/1); IR 3050, 1600 (Ph), 2700, 1705 (HC=O) cm^{-1}; ^1H NMR (60 MHz) δ 1.5–1.9 (m, 2 H, CH_2CH_2S), 2.2–2.6 (m, 4 H, $CH_2CH_2CH_2$), 3.6 (s, 2 H, CH_2Ph), 7.2 (s, 5 H, Ph), 9.8 (t, J = 1.5, HCO); MS 194 (M^+, 8), 92 (13), 91 (100), 65 (27). Anal. Calcd for $C_{11}H_{14}OS$; C, 68.00; H, 7.26. Found: C, 68.4; H, 7.1.

2,6-Nonanedione (30b):[54] t_r = 9.10 min (A), R_f = 0.33 (4/1); IR 1700 (C=O) cm^{-1}; ^1H NMR (60 MHz) δ 0.9 (t, J = 7, 3 H, CH_3CH_2), 1.4–1.9 (m, 4 H, CH_3CH_2, $CH_2CH_2CH_2$), 2.05 (s, 3 H, CH_3CO), 2.15–2.55 (m, 6 H, 3 CH_2CO); MS 156 (M^+, 2), 85 (20), 71 (38), 55 (14), 43 (100).

3(4-Oxopentyl)cyclohexanone (31b): t_r = 12.79 min (A), R_f = 0.45 (3/2); IR 1700 (C=O) cm^{-1}; ^1H NMR (60 MHz) δ 1.1–2.5 (m with a s at 2.05, all H); MS 182 (M^+, 1), 98 (100), 97 (84), 55 (34), 43 (100), 41 (36). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.3; H, 9.9.

4-Benzoylbutyrophenone (32c):[55] t_r = 10.99 min (C), R_f = 0.66 (4/1); IR 3040, 1590 (Ph), 1660 (C=O) cm^{-1}; ^1H NMR (300 MHz) δ 2.05 (t, J = 6.9, 2 H, CH_2CH_2CO), 2.95 (t, J = 6.9, 4 H, 2 CH_2CO), 7.25–7.85 (m, 10 H, 2 Ph); ^{13}C NMR δ 18.45, 37.3, 127.7, 128.4, 132.75, 136.55, 199.55; MS 252 (M^+, 5), 120 (12), 105 (100), 77 (91), 50 (17).

4-(Benzylthio)butyrophenone (33c): t_r = 11.54 min (C), R_f = 0.74 (4/1); mp 67 °C (hexane/ethyl acetate); IR (melted) 3040, 1580 (Ph), 1660 (C=O) cm^{-1}; ^1H NMR (300 MHz) δ 2.01 (t, J = 7.05, 2 H, CH_2CH_2S), 2.53 (t, J = 7.0, 2 H, CH_2CO), 3.05 (t, J = 7.15, 2 H, CH_2CH_2S), 3.71 (s, 2 H, CH_2Ph), 7.25–7.34 (m, 5 H, $PhCH_2$), 7.37–7.98 (m, 5 H, PhCO); ^{13}C NMR δ 23.3, 30.85, 36.05, 35.05, 126.9, 128.0, 128.45, 128.55, 128.8, 132.95, 136.9, 138.4, 199.5; MS 270 (M^+, 3), 179 (16), 150 (12), 105 (43), 91 (100), 77 (56).

In Situ Reaction of Hydroxytetrahydropyrans of the Type 27 with Silyl Derivatives. Isolation of Products 24a–40a, 41b, and 42b. The dioxolane (2.5 mmol) was first hydrolyzed according to the preceding general procedure. The crude hydrolyzed product was then dissolved in dry CH_2Cl_2 (15 mL) and cooled at −78 °C, and to the resulting solution was added triethylsilane, trimethylsilyl cyanide, or allyltrimethylsilane (5 mmol) and $BF_3{\cdot}Et_2O$ (7.5 mmol). The mixture was stirred for 1 h at the same temperature and overnight allowing the temperature to rise to 20 °C. Then, it was hydrolyzed with saturated aqueous $NaHCO_3$ (10 mL) and extracted with ether (2 × 10 mL) and the organic layer dried (Na_2SO_4). Solvents were removed in vacuo (15 Torr), and the resulting residue was purified by flash chromatography (silica gel; hexane/ether) to give the corresponding products **34a–40a**, **41b**, and **42b**. Yields are reported in Table III. Physical, spectral, and analytical data follow.

1-Oxaspiro[5.5]undecane (34a):[33] t_r = 8.05 min (B), R_f = 0.75 (19/1); IR 1080, 990 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.00–1.80 (m, 16 H, $(CH_2)_5C(CH_2)_3$), 3.57 (t, J = 5.35, 2 H, CH_2O); ^{13}C NMR δ 18.95, 21.6, 26.3, 26.35, 34.85, 35.6, 60.7, 71.75; MS 154 (M^+, 13), 111 (100), 98 (76), 86 (61), 84 (99), 43 (46).

6-Allyl-2,2-diethyltetrahydropyran (35a): t_r = 8.41 min (B), R_f = 0.67 (19/1); IR 3060, 1630 (HC=C), 1200, 1080 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 0.77, 0.82 (2 t, J = 7.5, 6 H, 2 CH_3), 1.05–1.85 (m, 10 H, 2 CH_3CH_2, 3 tetrahydropyran CH_2), 1.95–2.30 (m, 2 H, CH_2C=C), 3.30–3.50 (m, 1 H, CHO), 4.90–5.10 (m, 2 H, CH_2=CH), 5.75–5.95 (m, 1 H, CH=CH_2); ^{13}C NMR δ 7.05, 7.6, 19.4, 22.45, 31.9, 32.2, 32.4, 41.55, 69.2, 75.4, 115.95, 135,7; MS 154 (M^+ – 28, 9), 153 (79), 81 (57), 57 (100), 55 (36), 41 (30).

6-Allyl-5-oxaspiro[4.5]decane (36a): t_r = 9.02 min (B), R_f = 0.74 (19/1); IR 3060, 1630 (HC=C), 1080, 1010 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.05–1.90 (m, 14 H, $(CH_2)_4C(CH_2)_3$), 2.00–2.30 (m, 2 H, CH_2C=C), 3.25–3.45 (m, 1 H, CHO), 4.65–5.05 (m, 2 H, CH_2=CH), 5.65–5.85 (m, 1 H, CH=CH_2); ^{13}C NMR δ 21.25, 23.15, 24.3, 31.3, 32.6, 34.95, 41.25, 41.55, 71.3, 83.75, 115.9, 135.55; MS 180 (M^+, 1), 139 (50), 121 (100), 67 (67), 55 (59), 41 (81).

2-Allyl-1-oxaspiro[5.5]undecane (37a): t_r = 10.00 min (B), R_f = 0.43 (19/1); IR 3060, 1630 (HC=C), 1080, 990 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 0.80–2.30 (m, 18 H, 9 aliphatic CH_2), 3.30–3.60 (m, 1 H, CHO), 4.90–5.15 (m, 2 H, CH_2=CH), 5.80–6.00 (m, 1 H, CH=CH_2); ^{13}C NMR δ 19.3, 21.35, 21.7, 26.45, 29.75, 31.7, 35.55, 40.55, 41.6, 69.0, 72.15, 115.85, 136.0; MS 194 (M^+, 1), 135 (53), 81 (58), 67 (61), 55 (70), 41 (100).

2,2-Diethyltetrahydropyran-6-carbonitrile (38a): t_r = 9.34 min (B), R_f = 0.56 (19/1); IR 2240 (C≡N), 1190, 990 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 0.74, 0.78 (2 t, J = 7.5, 6 H, 2 CH_3), 1.25–1.90 (m, 10 H, 5 CH_2), 4.73 (dd, J = 9.5, 3.1, 1 H, CH); ^{13}C NMR δ 6.95, 7.25, 17.65, 23.8, 29.6, 30.35, 30.95, 59.8, 77.9, 119.35; MS 166 (M^+ – 1, <1), 139 (10), 138 (100), 111 (29), 57 (59), 55 (12), 41 (10). Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.24; N, 8.37. Found: C, 71.5; H, 10.2; N, 8.5.

5-Oxaspiro[4.5]decane-6-carbonitrile (39a): t_r = 10.01 min (B), R_f = 0.35 (19/1); IR 2240 (C≡N), 1210, 1010 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.30–2.20 (m, 14 H, 7 CH_2), 4.41 (dd, J = 9.5, 3.4, 1 H, CH); ^{13}C NMR δ 19.8, 23.4, 24.05, 29.8, 33.9, 40.0, 61.3, 85.95, 119.3; MS 165 (M^+, 13), 137 (12), 136 (85), 123 (100), 67 (30), 55 (56), 41 (27).

1-Oxaspiro[5.5]undecane-2-carbonitrile (40a): t_r = 10.92 min (B), R_f = 0.39 (19/1); IR 2240 (C≡N), 1140, 990 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.24–1.88 (m, 16 H, 8 CH_2), 4.48 (dd, J = 9.1, 3.25, 1 H, CH); ^{13}C NMR δ 17.6, 21.3, 21.45, 25.9, 29.9, 31.3, 34.25, 38.15, 59.55, 74.6, 119.5; MS 179 (M^+, 9), 137 (26), 136 (100), 123 (67), 55 (46), 41 (19).

***trans*-2-Phenyltetrahydropyran-6-carbonitrile (*trans*-41a)**:[56] t_r = 12.12 min (B), R_f = 0.30 (19/1); IR 3040, 1590 (Ph), 2240 (C≡N); 1080, 1030 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.50–2.10 (m, 6 H, 3 CH_2), 4.81 (dd, J = 11.55, 2.0, 1 H, CHCN), 4.95–5.05 (m, 1 H, CHPh), 7.25–7.45 (m, 5 H, Ph); ^{13}C NMR δ 20.05, 28.3, 32.6, 65.3, 76.6, 117.7, 126.0, 127.95, 128.45, 145.15; MS 187 (M^+, 31), 158 (25), 133 (18), 105 (100), 91 (22), 77 (51).

***cis*-2-Phenyltetrahydropyran-6-carbonitrile (*cis*-41a)**:[56] t_r = 12.42 min (B), R_f = 0.20 (19/1); IR the same as for *trans*-**41a**; ^1H NMR (300 MHz) δ 1.50–2.10 (m, 6 H, 3 CH_2), 4.35–4.40 (m, 2 H, 2 CHO), 7.25–7.45 (m, 5 H, Ph); ^{13}C NMR δ 23.1, 29.9, 32.5, 66.5, 80.8, 118.15, 125.75, 127.9, 128.4, 141.05; MS 187 (M^+, 28), 158 (23), 133 (21), 105 (100), 91 (21), 77 (51).

2-Allyl-2-methyl-1-oxaspiro[5.5]undecane (42b): t_r = 10.74 min (B), R_f = 0.77 (19/1); IR 3060, 1630 (HC=C), 1120, 1030 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.17 (s, 3 H, CH_3), 1.20–1.75 (m, 16 H, 8 ring CH_2), 2.20 (d, J = 7.1, 2 H, CH_2C=C), 4.95–5.05 (m, 2 H, CH_2=CH), 5.8–6.0 (m, 1 H, CH=CH_2); ^{13}C NMR δ 16.0,

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22.45, 22.75, 26.3, 27.8, 34.9, 35.0, 37.4, 40.9, 49.2, 72.2, 72.7, 116.5, 135.65; MS 208 (M^+, 1), 167 (61), 149 (100), 67 (46), 55 (30), 41 (44). Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.7; H, 11.3.

2-Methyl-1-oxaspiro[5.5]undecane-2-carbonitrile (43b): t_r = 10.47 min (B), R_f = 0.44 (19/1); IR 2240 (C≡N), 1080, 980 (CO) cm^{-1}; ^1H NMR (300 MHz) δ 1.15–2.10 (m with a s at 1.56, all H); ^{13}C NMR δ 16.8, 21.75, 22.0, 26.05, 30.25, 31.55, 34.5, 36.9, 41.25, 66.7, 75.45, 123.15; MS 194 (M^+, 2), 151 (38), 150 (100), 137 (98), 55 (39), 41 (34).

In Situ Oxidation of Hydroxytetrahydropyrans of the Type 27a. Isolation of δ-Lactones 44–57. For general procedure[18b] and details for the analytical and spectral characterization of compounds **44**,[57] **45**,[36] **46**,[38] **47**,[58] **48**, **49**, **50**,[59] **51**,[38] **52**, **53**, **54**,[38] **55**,[60] **56**,[33] and **57** (see eq 4), see the the supplementary material.

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Registry No. **4a**, 129471-18-7; **4b**, 133549-41-4; **4c**, 133549-42-5; **9a**, 16686-11-6; **9b**, 5978-08-5; **9c**, 3308-98-3; **10a**, 3390-13-4; **10b**, 4352-98-1; **10c**, 133549-21-0; **11a**, 130518-96-6; **11b**, 129847-08-1; **11c**, 133549-22-1; **12a**, 59985-72-7; **12b**, 56341-93-6; **12c**, 133549-23-2; **13a**, 133549-18-5; **13b**, 58568-17-5; **13c**, 133549-24-3; **14a**, 133549-19-6; **14b**, 58568-20-0; **14c**, 133549-25-4; **15a**, 129847-03-6; **15b**, 129847-09-2; **15c**, 133549-26-5; **16a**, 133549-20-9; **16b**, 53857-10-6; **17a**, 24175-21-1; **17b**, 42991-09-3; **18a**, 130518-97-7; **18b**, 38338-80-6; **19a**, 129847-04-7; **19b**, 944-27-4; **20a**, 129847-05-8; **20b**, 129847-10-5; **21a**, 129847-06-9; **21b**, 129864-57-9; **22a**, 129847-07-0; **22b**, 129847-11-6; **23**, 133549-37-8; **24a**, 78-94-4; **24b**, 930-68-7; **25a**, 75506-74-0; **25b**, 133549-27-6; **25c**, 133549-28-7; **26b**, 133578-17-3; **27a**, 133549-38-9; **28a**, 133549-38-9; **29a**, 133549-39-0; **30b**, 36452-81-0; **31b**, 133549-40-3; **32c**, 6263-83-8; **33c**, 133578-18-4; **34a**, 180-79-0; **35a**, 133549-29-8; **36a**, 133549-30-1; **37a**, 133549-31-2; **38a**, 133549-32-3; **39a**, 133549-33-4; **40a**, 133549-34-5; *cis*-**41a**, 124469-06-3; *trans*-**41a**, 124469-07-4; **42b**, 133549-35-6; **43b**, 133549-36-7; **44**, 28525-62-4; **45**, 705-86-2; **46**, 2610-95-9; **47**, 2319-32-6; **48**, 2610-93-7; **49**, 129665-07-2; **50**, 28771-65-5; **51**, 102540-91-0; **52**, 129665-08-3; **53**, 129665-09-4; **54**, 115407-73-3; **55**, 20127-07-5; **56**, 4481-78-1; **57**, 120375-26-0; DMF, 68-12-2; *i*-PrCHO, 78-84-2; PhCHO, 100-52-7; MeCOEt, 78-93-3; $(\overline{CH_2})_4CO$, 120-92-3; $(\overline{CH_2})_5CO$, 108-94-1; $(\overline{CH_2})_7CO$, 502-49-8; PhCOMe, 98-86-2; c-C_3H_5COPh, 3481-02-5; PhCN, 100-47-0; $PhCON(\overline{CH_2})_4$, 3389-54-6; PhCOCl, 98-88-4; PhNCS, 103-72-0; PhCHNPh, 538-51-2; $(PhCH_2S)_2$, 150-60-7; $PrCON(\overline{CH_2})_4$, 33527-93-4; EtOCOCl, 541-41-3; CuBr·Me_2S, 54678-23-8; EtCOEt, 96-22-0; *n*-$C_5H_{11}CHO$, 66-25-1; MeCOMe, 67-64-1; *i*-BuCOMe, 108-10-1; *t*-BuCOMe, 75-97-8; EtCOPh, 93-55-0; *n*-PrCOPh, 495-40-9; PhCOPh, 119-61-9; triethylsilane, 617-86-7; trimethylsilyl cyanide, 7677-24-9; allyltrimethylsilane, 762-72-1.

Supplementary Material Available: Full analytical and spectral data for compounds **10a**, **12a**, **17a**, **10b**, **13b**, **16b**, **17b**, **19b**, **25a**, **44–57**; experimental procedure for compounds **44–57**; and copies of ^1H (300 MHz) and ^{13}C (75 MHz) NMR of compounds **10c**, **11c–14c**, **25c**, **33c**, **35a–37a**, **39a**, **40a**, ***trans*-41a**, ***cis*-41a**, **43b**, **48**, **49**, **52**, and **53** (44 pages). Ordering information is given on any current masthead page.

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Cyclopentenyllithium Additions to Chiral Aldehydes. Diastereofacial Selectivity Indicating the Absence of a Pronounced Neighboring Carboxylate Anion Effect

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The 1,2-addition of cyclopentenyllithium to a series of three five-membered aldehydo esters and their hemiacylals has been examined in order to assess the level and direction of facial selectivity surrounding nucleophilic attack at the aldehyde carbonyl and to clarify possible electronic and steric contributions stemming from neighboring functional groups. Neither methyl substitution of the acetic acid (ester) side chain nor the interchange of ester for carboxylate anion serve as important diastereocontrol elements. Instead, diastereofacial selectivity in these and related cyclic carboxaldehydes is governed by the inherent structural features of the ring system to which the functional group is attached. The convenient preparation of a complete subset of isomerically pure bicyclic lactones carrying five stereogenic centers is reported.

Major uncertainties persist in understanding the diastereofacial selectivities associated with addition reactions involving *cyclic* carboxaldehydes. Sound predictive knowledge concerning, and reasonable control of, the stereochemical outcomes underlying such nucleophilic processes is an unsolved problem. The specific issue is exemplified by (+)-1, a compound believed to be blocked from nucleophilic capture along that direction cofacial with the dithioketal.[2] However, the illustrated Grignard addition proceeds with formation of a 1:1 mixture of **2** and **3**.

The three observations grouped in Scheme I hold similar interest. The addition of 3-furyllithium to aldehydo ester

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