99.6/0.4. The structures of the products were identified by ^1H NMR and IR spectroscopy after purification by preparative GC.

Dihydro-4,4-dimethyl-2(3*H*)-furanone (2a): ^1H NMR 1.19 (s, 6 H, Me), 2.32 (s, 2 H, 3-H), 3.97 (s, 2 H, 5-H); IR 1780 cm^{-1} (C=O).

Dihydro-4-methyl-2(3*H*)-furanone (2b): ^1H NMR 1.15 (d, 3 H, Me, J = 7 Hz), 2.0–2.8 (m, 3 H, 3-H, 4-H), 3.85, 4.41 (2 dd, 2 × 1 H, 5-H, J_{gem} = 9 Hz, J_{vic} = 6 Hz); IR 1780 cm^{-1} (C=O).

Dihydro-4-isopropyl-2(3*H*)-furanone (2c): ^1H NMR 0.90, 0.94 (2 d, 2 × 3 H, Me, J = 6 Hz), 1.4–1.9 (m, 1 H, $(CH_3)_2CH$), 2.0–2.6 (m, 3 H, 3-H, 4-H), 3.8–4.0, 4.25–4.45 (2 m, 2 × 1 H, 5-H); IR 1780 cm^{-1} (C=O).

Dihydro-4-phenyl-2(3*H*)-furanone (2d): ^1H NMR (400MHz) 2.69 (dd, 1 H, 3-H, J_{gem} = 17.4 Hz, J_{vic} = 9.2 Hz), 2.93 (dd, 1 H, 3-H, J_{gem} = 17.4 Hz, J_{vic} = 8.5 Hz), 3.75–3.84 (m, 1 H, 4-H), 4.28 (dd, 1 H, 5-H, J_{gem} = 9.2 Hz, J_{vic} = 7.6 Hz), 4.68 (fortuitous t, 1 H, 5-H, J_{gem} = 9.2 Hz, J_{vic} = 7.9 Hz), 7.18–7.41 (m, 5 H, C_6H_5); IR 1780 cm^{-1} (C=O).

Dihydro-4-methoxy-2(3*H*)-furanone (2e): ^1H NMR 2.4–2.85 (m, 2 H, 3-H), 3.34 (s, 3 H, Me), 4.1–4.4 (m, 3 H, 4-H, 5-H); IR 1775 cm^{-1} (C=O).

Dihydro-4-butoxy-2(3*H*)-furanone (2f): ^1H NMR 0.91 (t, 3 H, Me, J = 6 Hz), 1.15–1.8 (m, 4 H, $CH_3CH_2CH_2$), 2.35–2.85 (m, 2 H, 3-H), 3.42 (t, 2 H, CH_2CH_2O, J = 6 Hz), 4.1–4.4 (m, 3 H, 4-H, 5-H); IR 1780 cm^{-1} (C=O).

Dihydro-4-(benzyloxy)-2(3*H*)-furanone (2g): ^1H NMR 2.5–2.7 (m, 2 H, 3-H), 4.2–4.4 (m, 3 H, 4-H, 5-H), 4.48 (s, 2 H, $PhCH_2$), 7.2–7.4 (m, 5 H, C_6H_5); IR (KBr) 1780 cm^{-1} (C=O).

Dihydro-4-(methoxymethoxy)-2(3*H*)-furanone (2h): ^1H NMR 2.4–2.95 (m, 2 H, 3-H), 3.37 (s, 3 H, Me), 4.3–4.6 (m, 3 H, 4-H, 5-H), 4.66 (s, 2 H, OCH_2O); IR 1780 cm^{-1} (C=O).

Dihydro-3,3-dimethyl-2(3*H*)-furanone (3a): ^1H NMR 1.27 (s, 6 H, Me), 2.11 (t, 2 H, 4-H, J = 7 Hz), 4.26 (t, 2 H, 5-H, J = 7 Hz); IR 1770 cm^{-1} (C=O).

Dihydro-3-methyl-2(3*H*)-furanone (3b): ^1H NMR 1.28 (d, 3 H, Me, J = 6 Hz), 1.8–2.9 (m, 3 H, 3-H, 4-H), 4.1–4.5 (m, 2 H, 5-H); IR 1765 cm^{-1} (C=O).

Dihydro-3-isopropyl-2(3*H*)-furanone (3c): ^1H NMR 0.93, 1.04 (2 d, 2 × 3 H, Me, J = 7 Hz), 1.8–2.6 (m, 4 H, 3-H, 4-H, $(CH_3)_2CH$), 4.05–4.4 (m, 2 H, 5-H); IR 1765 cm^{-1} (C=O).

Dihydro-3-phenyl-2(3*H*)-furanone (3d): ^1H NMR (400 MHz) 2.40–2.51, 2.69–2.77 (2 m, 2 × 1 H, 4-H), 3.82 (fortuitous t, 1 H, 3-H, J_{vic} = 9.6 Hz, 9.6 Hz), 4.33–4.39, 4.46–4.52 (2 m, 2 × 1 H, 5-H), 7.26–7.40 (m, 5 H, C_6H_5); IR 1765 cm^{-1} (C=O).

Dihydro-3-methoxy-2(3*H*)-furanone (3e): ^1H NMR 2.1–2.8 (m, 2 H, 4-H), 3.54 (s, 3 H, Me), 3.95–4.5 (m, 3 H, 3-H, 5-H); IR 1780 cm^{-1} (C=O).

Dihydro-3-butoxy-2(3*H*)-furanone (3f): ^1H NMR 0.91 (t, 3 H, Me, J = 7 Hz), 1.15–2.0 (m, 4 H, $CH_3CH_2CH_2$), 2.0–2.8 (m, 2 H, 4-H), 3.4–4.5 (m, 5 H, 3-H, 5-H, CH_2CH_2O); IR 1780 cm^{-1} (C=O).

Dihydro-3-(benzyloxy)-2(3*H*)-furanone (3g): ^1H NMR 2.0–2.6 (m, 2 H, 4-H), 3.9–4.5 (m, 3 H, 3-H, 5-H), 4.69, 4.86 (AB signal, 2 H, $PhCH_2$, J = 12 Hz), 7.1–7.4 (m, 5 H, C_6H_5); IR 1780 cm^{-1} (C=O).

Dihydro-3-(methoxymethoxy)-2(3*H*)-furanone (3h): ^1H NMR 2.0–2.8 (m, 2 H, 4-H), 3.42 (s, 3 H, Me), 4.1–4.5 (m, 3 H, 3-H, 5-H), 4.71, 4.93 (AB signal, 2 H, OCH_2O, J = 6 Hz); IR 1790 cm^{-1} (C=O).

Tetrahydro-5,5-dimethyl-2*H*-pyran-2-one (5a): ^1H NMR 1.05 (s, 6 H, Me), 1.69 (t, 2 H, 4-H, J = 7 Hz), 2.55 (t, 2 H, 3-H, J = 7 Hz), 3.96 (s, 2 H, 6-H); IR 1735 cm^{-1} (C=O).

Tetrahydro-5-methyl-2*H*-pyran-2-one (5b): ^1H NMR 1.00 (d, 3 H, Me, J = 6 Hz), 1.3–2.3 (m, 3 H, 4-H, 5-H), 2.4–2.7 (m, 2 H, 3-H), 3.91 (dd, 1 H, 6-H, J_{gem} = 11 Hz, J_{vic} = 10 Hz), 4.28 (ddd, 1 H, J_{gem} = 11 Hz, J_{vic} = 4 Hz, ^4J = 2 Hz); IR 1730 cm^{-1} (C=O).

Tetrahydro-5-phenyl-2*H*-pyran-2-one (5c): ^1H NMR (400 MHz) 2.13–2.23 (m, 2 H, 4-H), 2.66 (ddd, 1 H, 3-H, J_{gem} = 18.0 Hz, J_{vic} = 7.4 Hz, 10.1 Hz), 2.78 (ddd, 1 H, 3-H, J_{gem} = 18.0 Hz, J_{vic} = 4.3 Hz, 6.7 Hz), 3.16–3.22 (m, 1 H, 5-H), 4.31 (fortuitous t, 1 H, 6-H, J_{gem} = 11.0 Hz, J_{vic} = 11.0 Hz), 4.48 (ddd, 1 H, 6-H, J_{gem} = 11.1 Hz, J_{vic} = 4.9 Hz, ^4J = 2.0 Hz), 7.24–7.38 (m, 5 H, C_6H_5); IR (KBr) 1730 cm^{-1} (C=O).

Tetrahydro-3,3-dimethyl-2*H*-pyran-2-one (6a): ^1H NMR 1.30 (s, 6 H, Me), 1.7–2.1 (m, 4 H, 4-H, 5-H), 4.35 (t, 2 H, 6-H, J = 5 Hz); IR 1730 cm^{-1} (C=O).

Tetrahydro-3-methyl-2*H*-pyran-2-one (6b): ^1H NMR 1.26 (d, 3 H, Me, J = 9 Hz), 1.4–2.3 (m, 4 H, 4-H, 5-H), 2.4–2.8 (m, 1 H, 3-H), 4.32 (t, 2 H, 6-H, J = 6 Hz); IR 1730 cm^{-1} (C=O).

Tetrahydro-3-phenyl-2*H*-pyran-2-one (6c): ^1H NMR (400 MHz) 1.93–2.14 (m, 3 H, 4-H, 5-H), 2.25–2.34 (m, 1 H, 4-H), 3.78 (dd, 1 H, 3-H, J = 9.7 Hz, 7.1 Hz), 4.41–4.51 (m, 2 H, 6-H), 7.20–7.40 (m, 5 H, C_6H_5).

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A Synthesis of 4-Oxo Carboxylic Acids, 4-Oxo Aldehydes, and 1,4-Diketones from γ-Lactones[1]

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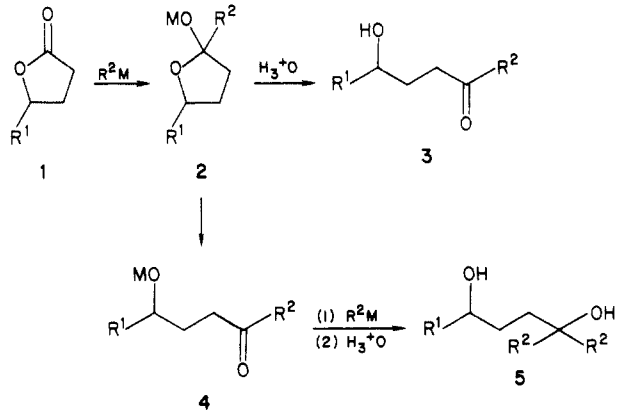
The α-methyldiphenylsilyl derivatives of γ-butyrolactone, γ-valerolactone, and the cis lactone of 2-hydroxycyclohexaneacetic acid have been reacted with Grignard reagents. The α-silylated lactones of γ-butyrolactone and γ-valerolactone react with a single equivalent of Grignard reagent to give a 2-substituted 4,5-dihydrofuran, which can be hydrolyzed and oxidized to 4-oxo carboxylic acids, 1,4-diketones, or 4-oxo aldehydes. The α-silylated fused lactone failed to react with ethylmagnesium bromide in refluxing tetrahydrofuran. An X-ray crystal structure of this silylated lactone indicated that this lack of reactivity is due to steric factors.

The preparation of 4-oxo acids, precursors to 5-substituted γ-lactones and of 1,4-diketones and 4-oxo aldehydes, valuable precursors to cyclopentenones, and important units in organic synthesis, as well as biologically and in-

0022-3263/86/1951-2039$01.50/0

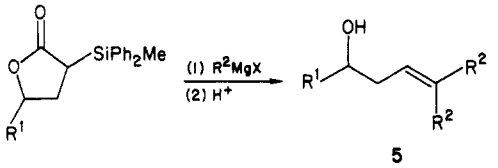
Scheme I



dustrially important systems,[4-6] remains an important endeavor. One seemingly straightforward approach to these systems would be the reaction of γ-lactones with a single equivalent of an organometallic reagent followed by oxidation of the resulting 4-hydroxy ketone. The problem with this approach lies in the difficulty of controlling the reaction to a single addition, the principal product usually being the diol (Scheme I).[7] Some success has been reported with the reaction of γ-lactones with organolithium reagents,[8] in particular ethynyllithium reagents.[9] The reaction of γ-lactones with Grignard reagents on the other hand has not met with success.[10] The key to the synthesis of 4-hydroxy ketones from γ-lactones and Grignard reagents is to prevent the opening of intermediate **2** to 4-oxido ketone **4**, which could then react with a second equivalent of Grignard reagent.

Results and Discussion

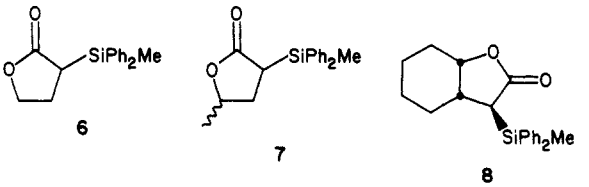
At the outset of this work we had encountered, in a separate study, excellent success in the conversion of ethyl (trimethylsilyl)acetate and ethyl (diphenylmethylsilyl)-acetate into 1,1-disubstituted alkenes via their reaction with Grignard reagents and an acid- or base-catalyzed elimination,[11] and we therefore anticipated the reaction of α-(diphenylmethylsilyl) γ-lactones as leading to the preparation of homoallylic alcohols according to eq 1.



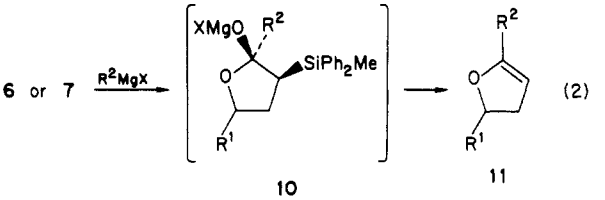
(1)

Lending to the attractiveness of this conversion was the ready availability of the α-(diphenylmethylsilyl) γ-lactones **6** and **7**, which can be prepared by direct C-diphenylmethylsilylation of the corresponding lithium enolate of the lactone according to our published procedure.[12,13b] On the other hand we fully realized that the possibility of attack of the organometallic reagent trans to the bulky diphenylmethylsilyl group would lead to intermediate **10** and that the cis-β-oxido organosilane could eliminate diphenylmethylsilyl oxide to produce the dihydrofuran **11** (eq 2). In addition direct attack of the organometallic reagent on silicon to generate the enolate was considered a possibility.

Preparation of α-Silyl Lactones. We concentrated our study on the three α-silyl γ-lactones, **6–8**, all of which were prepared in excellent yield via diphenylmethylsilylation of the appropriate lithium lactone enolate.[12,13b]



Lactone **7** was prepared as an approximate 60:40 mixture of diastereomers, which was reacted as the mixture. The preparation of **8** gave a single diastereomer, which we have assigned the structure shown based on the assumption that silylation takes place from the β-face of the enolate.[13] This assumption was shown to be correct by an X-ray diffraction study (vide infra).



(2)

Preparation of 2-Substituted 4,5-Dihydrofurans. Treatment of α-silyl lactone **7** with a twofold excess of propylmagnesium bromide in refluxing THF for 16 h and careful workup with aqueous sodium bicarbonate gave a crude product that showed bands at 1690 and 1665 cm^{-1} in the infrared spectrum and a multiplet at 4.4 ppm in the

(1) The chemistry of α-Silyl Carbonyl Compounds. 12. For parts 10 and 11, see: Larson, G. L. *Synth. Commun.*, in press.

(2) Graduate students funded on MBRS Grant RR-8102-10. Taken in part from the Ph.D. Dissertations of R. M. B. de P. and L. M. Fuentes, The University of Puerto Rico—Rio Piedras Campus, 1984 and 1982, respectively.

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(4) For reviews, consult: (a) Ellison, R. A. *Synthesis* **1973**, 397. (b) Grobel, B.-T.; Seebach, D. *Ibid.* **1977**, 357. (c) Ho, T.-L. *Synth. Commun.* **1974**, *4*, 265. In the synthesis of prostaglandins: (d) Axen, U.; Pike, J. E.; Schneider, W. P. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1973; Vol. 1, p 81. (e) Bindra, J. S. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1981; Vol. 4, p 353. (f) Bindra, J. S.; Bindra, R. *Prostaglandin Synthesis*; Academic: New York, 1977. (g) Mitra, A. *The Synthesis of Prostaglandins*; Wiley: New York, 1977; pp 233–278.

(5) For some syntheses of 4-oxo aldehydes, consult: (a) Stowell, J. C. *J. Org. Chem.* **1976**, *40*, 560. (b) Yoshida, T.; Saito, S. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3047. (c) Oshima, K.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1973**, *95*, 4446. (d) Matsuda, I.; Murata, S.; Izumi, Y. *J. Org. Chem.* **1980**, *45*, 237. For the preparation of 4-hydroxy ketones, consult: (e) Larcheveque, M.; Valette, G.; Cuvigny, T.; Normant, H. *Synthesis* **1975**, 256. (f) Carachioli, S.; Savoia, D.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1984**, 49, 1246 and references therein.

(6) For some of the more recent syntheses of 1,4-diketones, consult: (a) Lepage, L.; Lepage, Y. *Synthesis* **1983**, 1018. (b) Duhamel, P.; Poirier, J. M.; Tavel, A. *Tetrahedron Lett.* **1984**, *25*, 43. (c) Barco, A.; Benetti, S.; Pollini, G. P.; Baraldi, P. G.; Guarneri, M.; Vicentini, C. B. *J. Org. Chem.* **1979**, *44*, 105. (d) Murata, S.; Matsuda, J. *Synthesis* **1978**, 221. (e) Sum, P.-E.; Weiler, L. *Can. J. Chem.* **1978**, *56*, 2301.

(7) See, for example: Vozza, J. F. *J. Org. Chem.* **1959**, *24*, 720.

(8) For some success with organolithium reagents, consult: (a) Reference 4f. (b) Savioa, D.; Trombini, C.; Unami-Ronchi, A. *Ibid.* **1982**, *47*, 564. (c) Musatto, M. C.; Savoia, D.; Trombini, C.; Umani-Ronchi, A. *Ibid.* **1980**, *45*, 4002. (d) Sanchez, E. L.; Arzeno, H. *Rev. Latinoam. Quim.* **1976**, *7*, 143. (e) Arzeno, H. B.; Sanchez, E. L. *Ibid.* **1979**, *10*, 65. (f) Kondo, K.; Tunemoto, D. *Tetrahedron Lett.* **1975**, 1397.

(9) Ethynyllithium reagents have been shown to monoadd to γ-lactones: (a) Olgura, H.; Takahashi, H.; Itoh, T. *J. Org. Chem.* **1972**, *37*, 72. (b) Phillips, C.; Jacobson, R.; Abrahams, B.; Williams, H. J.; Smith, L. R. *Ibid.* **1980**, *45*, 1920. (c) Jacobson, R.; Taylor, R. J.; Williams, H. J.; Smith, L. R. *Ibid.* **1982**, *47*, 3140. (d) Larock, R. C.; Liu, C.-L. *Ibid.* **1983**, *48*, 2151. (e) Chabala, J. C.; Vincent, J. E. *Tetrahedron Lett.* **1978**, 937.

(10) Methylmagnesium bromide works well with a very hindered steroidal lactone: Baddeley, G. V.; Carpio, H.; Edwards, J. A. *J. Org. Chem.* **1966**, *31*, 1026.

(11) Larson, G. L.; Hernandez, D. *Tetrahedron Lett.* **1982**, *23*, 1035.

(12) Larson, G. L.; Fuentes, L. M. *J. Am. Chem. Soc.* **1981**, *103*, 2418.

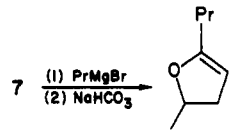
(13) (a) Grieco, P. A.; Miyashita, M. *J. Org. Chem.* **1974**, *39*, 120. (b) Larson, G. L.; Betancourt de Perez, R. *Ibid.* **1985**, *50*, 5257.

Table I. 4-Oxo Carboxylic Acids from α-(Diphenylmethylsilyl) γ-Butyrolactone[a]

entry	grignard reagent	product	% yield[b]
1	CH_3MgI	$HO_2C(CH_2)_2COCH_3$	71[c]
2	CH_3CH_2MgBr	$HO_2C(CH_2)_2COCH_2CH_3$	73[d]
3	n-$C_5H_{11}MgBr$	$HO_2C(CH_2)_2CO$-n-C_5H_{11}	83[e]
4	PhMgBr	$HO_2C(CH_2)_2COPh$	75[f]
5	$PhCH_2MgCl$	$HO_2C(CH_2)_2COCH_2Ph$	78[g]
6	$(CH_3)_3CMgCl$	$HO_2C(CH_2)_2CO_2H$	75[h]
7	$(CH_3)_2CHCH_2$-MgBr	$HO_2C(CH_2)_2COCH_2CH(CH_3)_2$	25[i]
8	c-$C_6H_{11}MgBr$	$HO_2C(CH_2)_2CO$-c-C_6H_{11}	50[j]

[a] According to eq 4. [b] Isolated yields. [c] Mp 32–34 °C (lit. mp 33–35 °C). *Dictionary of Organic Compounds*, Heilbron, I., Ed.; 1965; Vol. 4, p 2594. [d] Mp 39–40 °C (lit. mp 40 °C). See ref *c*, p 2590. [e] Mp 69–70 °C (lit. mp 70–71 °C). See ref *c*, p 2591. [f] Mp 115–116 °C (lit. mp 115–115.5 °C). Russell, R. R.; Vanderwerf, C. A. *J. Am. Chem. Soc.* **1947**, *69*, 11. [g] Mp 54–55 °C (lit. mp 55–56 °C). See ref *c*, p 2594. [h] Mp 185–187 °C (lit. mp 185 °C). See ref *c*, Vol. 5, p 2926. [i] Compound was only about 85% pure. [j] Compound was very impure.

^1H NMR spectrum, consistent with the formation of 2-propyl-4,5-dihydrofuran **12**. Also present, as evidenced



(3)

12

by ^1H NMR spectroscopy, were diphenylmethylsilanol and *sym*-tetraphenyldimethylsiloxane. Although spectral analyses of the crude reaction product indicated a high conversion to **12**, material contaminated with a small amount of ether could be obtained by distillation in only 50% yield (eq 3). Clearly the reaction is proceeding through attack trans to the diphenylmethylsilyl group, leading directly to the dihydrofuran, which is inert to the reaction conditions. Unfortunately, however, we were unable to prepare and purify other less volatile 5-substituted 4,5-dihydrofurans, the difficulty being in separating them from the diphenylmethylsilanol and disiloxane side products formed in the reaction. All attempts to purify the dihydrofurans, including low-temperature column chromatography on deactivated silica gel and alumina resulted in decomposition. Attempts to render the diphenylmethylsilanol more mobile on the column by trimethylsilylation of the reaction mixture prior to workup, to prepare *unsym*-diphenyltetramethyldisiloxane, resulted in decomposition of the dihydrofuran.

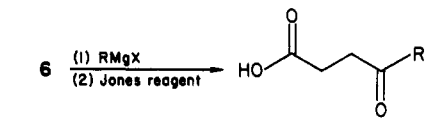
The reaction of α-silyl lactone **6** with butyllithium in THF gave several products, among which was butylmethyldiphenylsilane, the result of attack at silicon by the lithium reagent. The reaction of **6** and **7** with organolithium reagents was not investigated further.

Preparation of 4-Oxo Carboxylic Acids. Although it did not prove possible to isolate the dihydrofurans in pure form it was felt that the crude materials would nevertheless be useful precursors to other products. Our first attempts along these lines was the direct oxidation to 4-oxo acids.[14] Reaction of **6** with an excess of methylmagnesium iodide in refluxing THF followed by workup and direct oxidation of the crude product with Jones reagent in acetone gave levulinic acid in less than 20% yield. Better results were obtained when the oxidation step was carried out in the two-phase ether–water solvent mixture, but the best results were obtained with Jones reagent in benzene–water[15] (eq 4). The results of the reaction of Grignard reagents with **6** followed by oxidation to the 4-oxo acids are given in Table I.

Table II. 4-Oxo Aldehydes and 1,4-Diketones from α-(Diphenylmethylsilyl) γ-Butyro- and γ-Valerolactones[a]

entry	lactone	grignard reagent	product R^1	product R^2	% yield[b]
1	6	n-C_6H_{13}	H	n-C_6H_{13}	52[c]
2	6	n-C_9H_{19}	H	n-C_9H_{19}	66[d]
3	6	i-C_4H_9	H	i-C_4H_9	49[e]
4	7	CH_3	CH_3	CH_3	52[f]
5	7	n-C_6H_{13}	CH_3	n-C_6H_{13}	75[g]
6	7	n-C_8H_{17}	CH_3	n-C_8H_{17}	89[h]
7	7	n-C_9H_{19}	CH_3	n-C_9H_{19}	98[i]
8	7	i-C_4H_9	CH_3	i-C_4H_9	62[j]
9	7	CH_2=CH	CH_3	CH_2CH_2CH=CH_2	42[k]
10	7	n-C_3H_7C≡C	CH_3	n-C_3H_7C≡C	46[l]
11	7	$PhCH_2$	CH_3	$PhCH_2$	49[m]
12	7	Ph	CH_3	Ph	63[n]

[a] According to eq 5. [b] Isolated yields. [c] Mp 66–68 °C; IR and ^1H NMR compared to those published. Oshima, K.; Yamamoto, H.; Nazaki, H. *J. Am. Chem. Soc.* **1973**, *95*, 4446. [d] Mp 64–65 °C (lit. liquid). IR and ^1H NMR compared to those published. Yoshida, T.; Saito, S. *Bull. Soc. Chem. Jpn.* **1982**, *55*, 3047. [e] IR and ^1H NMR compared to those published. Cazes, B., Julia, S. *Bull. Chem. Soc. Fr.* **1977**, 931. [f] IR spectrum compared to that published. Pouchert, C. J. *The Aldrich Library of Infrared Spectra*, 3rd ed.; Aldrich: Milwaukee, 1981; p 252A. [g] Mp 33 °C (lit. mp 33–34 °C). Mukaiyama, T.; Narasaka, K.; Furusato, M. *J. Am. Chem. Soc.* **1972**, *94*, 8641. [h] Mp 45–47 °C; ^1H NMR compared to that published. Watanabe, S.; Fujita, T.; Suga, K.; Haibara, M. *Aust. J. Chem.* **1982**, *35*, 1739. [i] Mp 51–53 °C (lit. mp 52–53 °C). Stetter, H.; Kuhlmann, H. *Tetrahedron Lett.* **1974**, 4505. [j] Bp 97 °C (9 mmHg) [lit. bp 51 °C (1 mmHg)]. Larcheveque, M.; Valette, J. Cuvigny, T.; Normant, H. *Synthesis* **1975**, 256. [k] See eq 6. [l] Product only about 85% pure. [m] Initial product was a mixture of cyclic (major) and acyclic material. Treatment of this mixture with 1% sodium hydroxide converted it completely to 3-methyl-2-phenylcyclopentenone. Ningirawath, S.; Ritchie, E.; Taylor, W. C. *Aust. J. Chem.* **1976**, *29*, 339. [n] ^1H NMR compared to that published. Mukaiyama, T. Narasaka, K.; Furusato, M. *J. Am. Chem. Soc.* **1972**, *94*, 8641.



(4)

As can be seen the reaction proceeds well with unhindered Grignard reagents producing the expected 4-oxo acid in excellent isolated yields. Treatment of **6** with isopropylmagnesium bromide gave no reaction, but **6** did react with isobutylmagnesium bromide to give the corresponding oxo acid albeit in diminished yield. The reaction with cyclohexylmagnesium bromide gave some of the desired product, but in a very impure state. The reaction with *tert*-butylmagnesium bromide gave adipic acid as a result of reduction of the carbonyl.

Preparation of 4-Oxo Aldehydes and 1,4-Diketones. Direct treatment of the crude dihydrofuran with pyridinium chlorochromate in dichlormethane gave the desired 4-oxo aldehyde in extremely low yield. It was felt that better results might be obtained by hydrolysis of the dihydrofuran to the 4-hydroxy ketone prior to the oxidation step, which in this case required a nonaqueous oxidation. Thus, **6** was treated with hexylmagnesium bromide and the crude product of this reaction treated with 10% aqueous hydrochloric acid for 2 h. This reaction was worked up, dried, and the concentrated and the crude

(14) This work has been communicated. Fuentes, L. M.; Larson, G. L. *Tetrahedron Lett.* **1982**, *23*, 271.

(15) Ogura, H.; Takahashi, H.; Itoh, Y. *Ibid.* **1972**, *38*, 3229.

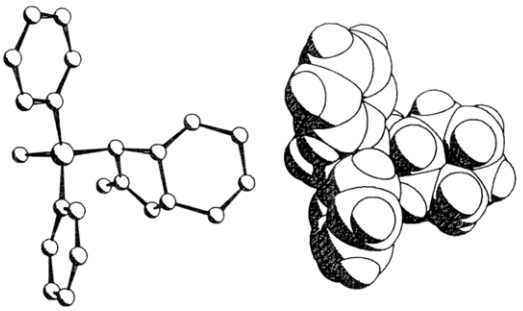
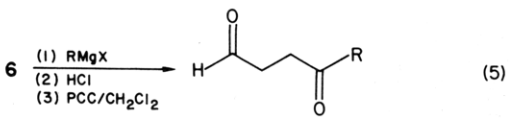


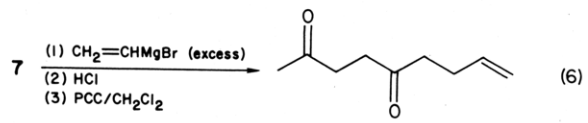
Figure 1.

4-hydroxy ketone directly oxidized with pyridinium chlorochromate[16] in dichloromethane to provide 4-oxodecanal in 52% yield (eq 5). As can be seen from the results shown in Table II (entries 1–3), similar results were obtained with nonylmagnesium bromide and isobutylmagnesium bromide.



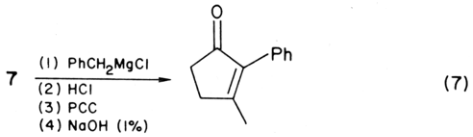
(5)

The application of this same procedure to the preparation of 1,4-diketones from lactone **7** gave similar results as can be seen from Table II (entries 4–12). The reaction with hexylmagnesium bromide provides the precursor to dihydrojasmone in 75% yield (entry 5). The reaction with vinylmagnesium bromide is interesting in that it gives bis addition of the Grignard reagent with the second equivalent adding in a Michael fashion to give 5,8-dioxonon-1-ene in 42% yield[17] (entry 9) (eq 6). Apparently in this system the intermediate **10** can open prior to elimination and the second equivalent of vinylmagnesium bromide readily Michael adds to the resulting enone.



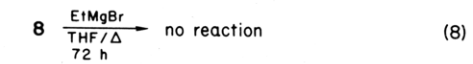
(6)

The reaction of **7** with benzylmagnesium chloride followed by oxidation gave mostly 2-phenyl-3-methylcyclopentenone together with a lesser amount of the acyclic material. Treatment of this mixture with 1% sodium hydroxide provided the cyclopentenone cleanly (eq 7).



(7)

Reaction of Ethylmagnesium Bromide with 8. Refluxing a 0.5 M solution of lactone **8** and 4 equiv of ethylmagnesium bromide in THF for 72 h gave no reaction (eq 8). An investigation of models of **8** indicated that the



(8)

carbonyl in this lactone was protected on the one side by the fused cyclohexane ring system and on the other by the rather bulky diphenylmethylsilyl group and was therefore inert to the Grignard reagent. An X-ray crystal structure determination on **8** showed this to be the case. The ball and stick and space-filling plots of the structure are shown in Figure 1.[18]

Experimental Section

General Considerations. All reactions were carried out in a standard apparatus consisting of a round-bottomed flask equipped with magnetic stirring, a reflux condenser, a no-air stopper and a nitrogen inlet. The apparatus was either flame-dried under a stream of nitrogen and allowed to cool under nitrogen or oven-dried for a minimum of 4 h and cooled under nitrogen prior to use. Room temperature was about 30 °C. Lactones **6–8** were prepared according to our published procedures.[13b] NMR spectra were recorded on Jeol FX90Q spectrometer and are reported with respect to internal tetramethylsilane. Mass spectra were recorded on a Hewlett-Packard 5995A spectrometer and are reported as m/e (relative abundance).

General Procedure for the Preparation of 4-Oxo Acids. A 250-mL, three-necked Morton flask equipped with magnetic stirring bar, an efficient condenser, and an addition funnel was charged with 10 mmol of **6** diluted in dry ether such as to make the ultimate solution 1 M in Grignard reagent. The Grignard solution (in excess as indicated) was added, and the reaction mixture stirred for 24 h. The excess Grignard reagent was destroyed by the slow addition of 10 mL of water at 0 °C. The reaction mixture was diluted with 10 mL of benzene and oxidized by the addition of 30 mmol of chromic acid solution[14] for 2 h. The organic layer was removed and washed with 10 mL of 3 N sodium hydroxide. The aqueous layer was acidified with 1.5 N hydrochloric acid to pH 1 (litmus paper). This aqueous solution was extracted with ether and the organic layer dried over anhydrous magnesium sulfate. Removal of the solvents in vacuo gave the acid as a crude solid, which was crystallized from dry hexane.

4-Oxohexanoic Acid: Representative Procedure. The standard apparatus of 250-mL capacity was charged with 2.82 g (10 mmol) of **6** and 25 mL of ether followed by the slow addition of 30.0 mL (30 mmol) of a 1.0 M ethylmagnesium bromide solution in ether. The reaction mixture was stirred at room temperature for 24 h, cautiously hydrolyzed by the addition of water (10 mL) at 0 °C, diluted with benzene (10 mL), and then titrated with chromic acid solution until the aqueous phase remained orange. The organic layer was extracted with 3 N sodium hydroxide (10 mL) and the aqueous layer acidified to pH 3 with 1.5 N hydrochloric acid. The aqueous layer was then extracted with ether (2 × 25 mL), dried over anhydrous sodium sulfate, and concentrated in vacuo to give the crude keto acid, which was crystallized from hexane to give 0.94 g (72.3%) of the title oxo acid.

4-Oxo-6-methylheptanoic Acid. Following the procedure above employing isobutylmagnesium bromide gave the title oxo acid: IR 1705 cm^{-1}; ^1H NMR δ 9.52 (br s, 1 H), 2.59 (m, 2 H), 2.23 (m, 2 H), 2.0 (br m, 2 H), 0.84 (d, 6 H, J = 6.4 Hz) [smaller peaks due to impurities were observed at 1.15, 1.08, and 0.94 ppm]; ^{13}C NMR δ 208.68, 178.49, 51.76, 37.46, 27.77, 24.77, 22.56.

4-Oxo-4-cyclohexylbutyric Acid. This product proved to be very impure and was not characterized. It showed the characteristic carbonyl stretch at 1705 cm^{-1} and the downfield acid proton, but the rest of the NMR spectrum was very complicated due to the impurities.

Preparation of 4-Oxo Aldehydes and 1,4-Diketones: General Procedure. A 100-mL, round-bottomed flask equipped with magnetic stirring bar, condenser, and nitrogen inlet was charged with 5 mmol of the silylated lactone **6** or **7**, 5 mL of THF, and an excess of an ether solution of Grignard reagent as indicated. The reaction mixture was refluxed for 12 h, after which time 25 mmol of chlorotrimethylsilane was added to silylate the diphenylmethylsilyl oxide produced and thus facilitate product isolation. The reaction mixture was then diluted with hexane and this solution treated with 1 M hydrochloric acid until the organic layer clarified. The aqueous layer was extracted with hexane (2 × 5 mL), and the combined organic layers were washed

(16) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

(17) We have observed the addition of 2 equiv of vinylmagnesium bromide, the second in a Michael fashion, to ethyl 2-methyl-2-(diphenylmethylsilyl)propionate. Larson, G. L.; Montes de Lopez-Cepero, I.; Torres, L. M. *Tetrahedron Lett.* **1984**, *25*, 1673. Larson, G. L.; Hernandez, D.; Montes de Lopez-Cepero, I.; Torres, L. E. *J. Org. Chem.* **1986**, *50*, 5260.

(18) Motherwell, W. D. S. Pluto, Program for plotting molecular and crystal structures, University of Cambridge, England, 1976.

with 10% sodium bicarbonate (5 mL) and dried over anhydrous magnesium sulfate. The solvents were removed in vacuo, and the resulting crude hydroxy ketone was oxidized directly with 1.6 g (7.5 mmol) of pyridinium chlorochromate in 10 mL of dichloromethane for 4 h. The reaction mixture was diluted with anhydrous ether (2 × 10 mL) and filtered through Florisil. The crude product was purified by column chromatography or crystallization.

Preparation of 4-Oxodecanal. Following the general procedure above 10 mmol of **6** was reacted with 28 mmol of hexylmagnesium bromide to yield 0.87 g (52%) of the title keto aldehyde: mp 66–68 °C (hexane); IR 1735, 1715 cm^{-1}; ^1H NMR δ 9.85 (s, 1 H), 2.74–2.55 (m, 4 H), 2.44 (t, 2 H, J = 7.3 Hz), 1.73–1.15 (m, 8 H), 0.88 (t, 3 H, J = 5.6 Hz); ^{13}C NMR δ 209.0, 178.6, 42.7, 36.7, 31.5, 28.8, 27.8, 23.7, 22.4, 13.9; MS, 170 (3), 98 (100).

Preparation of 2,5-Undecanedione. Representative 1,4-Diketone Synthesis. The standard apparatus was charged with 2.96 g (10 mmol) of **7**, 10 mL of THF, and 29 mL (28.1 mmol) of 0.97 M hexylmagnesium bromide in THF. The resulting solution was heated to reflux for 12 h and worked up as above. The crude reaction product was purified by alumina chromatography eluting with 2% ethyl acetate/hexane to give 1.38 g (75%) of the title dione.

Preparation of 5,8-Dioxonon-1-ene. A standard apparatus was charged with 15 mL (15 mmol) of a 1.0 M THF solution of vinylmagnesium bromide and 1.48 g (5 mmol) of **7** in 5 mL of THF. The reaction mixture was heated to reflux for 12 h, diluted with hexane (20 mL), and treated with 1 N hydrochloric acid until the organic layer clarified. The aqueous layer was extracted with hexane (2 × 5 mL), and the combined organic layers were dried over anhydrous magnesium sulfate. The organic layer was then filtered, and the solvents were removed in vacuo. The crude hydroxy ketone was dissolved in dichloromethane (5 mL) and oxidized with pyridinium chlorochromate in 10 mL of dichloromethane over a 4-h period. The reaction mixture was diluted with ether (20 mL) and filtered through a small plug of Florisil. The crude product was purified by trap-to-trap distillation to give 0.32 g (42%) of the title dione: IR 1718, 1710, 1635 cm^{-1}; ^1H NMR δ 6.07–5.5 (m, 1 H), 5.19–4.88 (m, 2 H), 2.69 (s, 4 H), 2.60–2.20 (m, 4 H), 2.18 (s, 3 H); ^{13}C NMR δ 208.4, 206.9, 136.9, 134.7, 41.7, 36.8, 36.1, 29.8, 27.7; MS, 154 (3), 99 (100).

Preparation of 6,9-Dioxodec-4-yne. Following the general procedure above 1.18 g (4 mmol) of **7** in 4 mL of THF was treated with 15 mL (12 mmol) of a 0.8 M solution of 1-pentynylmagnesium bromide (prepared from ethylmagnesium bromide and 1-pentyne) in THF. Vacuum distillation of the crude product gave 0.31 g (46%) of the title diketone in about 85% purity: bp 154 °C (2 mmHg); IR 1220, 1720, 1670 cm^{-1}; ^1H NMR 3.05–2.70 (m, 4 H), 2.34 (t, 2 H, J = 6.8 Hz), 1.81–1.37 (m, 2 H), 1.02 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 202.6, 185.8, 94.6, 80.4, 38.7, 36.3, 29.2, 20.8, 20.4, 13.0; MS, 166 (2), 95 (100).

X-ray Crystal Structure. The crystal chosen for data collection was a cut fragment 0.5 × 0.5 × 0.32 mm in size. Preliminary examination on the diffractometer indicated the monoclinic space groups $C2/c$ or Cc by systematic absences. The space group $C2/c$ was chosen as the more likely, as was proven correct by the structure solution. Data was collected on an Enraf-Nonius CAD-4 diffractometer fitted with a liquid nitrogen low-temperature device and using Mo K$\bar{\alpha}$ radiation (λ = 0.71069 Å). The cell dimensions at 138 K are a = 17.445 (6) Å, b = 9.981 (4) Å, c = 21.727 (10) Å, and β = 107.29 (5)° for Z = 8, as determined by refining the 2θ angles for 25 reflections in the range $20° < 2\theta < 28°$. A total of 3144 unique reflections were collected to a 2θ limit of 50°, with 2744 considered observed ($I > 2\sigma(I)$). Standard reflections measured after every 150 reflections indicated no crystal deterioration. The data was corrected for Lorentz and polarization effects, but no absorption correction was applied (μ = 1.02 cm^{-1}). The structure was solved by direct methods with SHELX.[19] After initial refinement of the non-hydrogen atom positions, the hydrogen atoms were refined with anisotropic thermal parameters; the hydrogen atom positional parameters were refined with fixed temperature factors (U = 0.03 Å^2). The function minimized during refinement was $\sum w(|F_o| - |F_c|)^2$, with $w = 1/\sigma(F)$. Atomic scattering factors and anomalous-dispersion corrections were from *International Tables for X-ray Crystallography* (1974);[20] all calculations were performed with SHELX.[19] The final refinement parameters, for all data, are R = 0.0521, R_w = 0.0530, and S (goodness of fit) = 2.93. A final difference map was essentially featureless, with e^-(max/min) = +/−0.3. Final atomic coordinates are given in the supplementary material accompanying this paper. Tables of anisotropic thermal parameters and hydrogen atom coordinates have been deposited as supplementary material.

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Registry No. **6**, 77772-24-8; **7** (isomer 1), 101914-27-6; **7** (isomer 2), 101914-28-7; **8**, 101773-27-7; **12**, 101773-29-9; CH_3MgI, 917-64-6; CH_3CH_2MgBr, 925-90-6; n-$C_5H_{11}MgBr$, 693-25-4; $PhMgBr$, 100-58-3; $PhCH_2MgCl$, 6921-34-2; $(CH_3)_3CMgCl$, 677-22-5; $(CH_3)_2CHCH_2MgBr$, 926-62-5; c-$C_6H_{11}MgBr$, 931-50-0; $HO_2C(CH_2)_2COCH_3$, 123-76-2; $HO_2C(CH_2)_2COCH_2CH_3$, 1117-74-4; $HO_2C(CH_2)_2CO$-n-C_5H_{11}, 6064-52-4; $HO_2C(CH_2)_2COPh$, 710-11-2; $HO_2C(CH_2)_2COCH_2Ph$, 54680-53-4; $HO_2C(CH_2)_2CO_2H$, 110-15-6; $HO_2C(CH_2)_2COCH_2CH(CH_3)_2$, 60856-79-3; $HO_2C(CH_2)_2CO$-c-C_6H_{11}, 15971-95-6; n-$C_9H_{19}MgBr$, 39691-62-8; n-$C_8H_{17}MgBr$, 17049-49-9; CH_2=$CHMgBr$, 1826-67-1; n-C_3H_7C≡$CMgBr$, 41246-05-3; n-$C_6H_{13}CO(CH_2)_2CHO$, 43160-78-7; n-$C_9H_{19}CO(CH_2)_2CHO$, 77328-83-7; i-$C_4H_9CO(CH_2)_2CHO$, 66471-61-2; $CH_3CO(CH_2)_2COCH_3$, 110-13-4; n-$C_6H_{13}CO(CH_2)_2COCH_3$, 7018-92-0; n-$C_8H_{17}CO(CH_2)_2COCH_3$, 32781-67-2; n-$C_9H_{19}CO(CH_2)_2COCH_3$, 51575-17-8; i-$C_4H_9CO(CH_2)_2COCH_3$, 53626-90-7; $CH_3CO(CH_2)_2COCH_2CH_2CH$=$CH_2$, 5312-86-7; n-C_3H_7C≡$CCO(CH_2)_2COCH_3$, 101773-28-8; $PhCH_2CO(CH_2)_2COCH_3$, 32776-14-0; $PhCO(CH_2)_2COCH_3$, 583-05-1; n-C_3H_7MgBr, 927-77-5.

Supplementary Material Available: Tables of anisotropic thermal parameters and hydrogen atom coordinates for compound **8** (3 pages). Ordering information is given on any current masthead page.

(19) Sheldrick, G. M. Shelx76, Program for crystal structure determination, University of Cambridge, England, 1976.
(20) *International Tables for X-ray Crystallography*; Kynoch: Birmingham, England, 1974.