^{1}H NMR (DMSO-d_6) δ 0.84 (s, 3 H), 0.91 (s, 3 H), 1.3–1.4 (m, 3 H), 1.45–1.6 (m, 3 H), 2.23–2.28 (m, 2 H), 2.29–2.32 (m, 2 H), 6.17 (br s, 2 H), 8.67 (d, J = 13 Hz, 1 H)]; 4-ethylcycloheptanone semicarbazone[18] (11) [37%; ca. 1:1 mixture of Z/E isomers by ^{13}C NMR; mp 128–130 °C (lit.[18] mp 125–127 °C); ^{1}H NMR δ 0.89 (t, J = 2 Hz, 3 H), 1.1–1.4 (m, 4 H), 1.4–1.5 (m, 1 H), 1.55–1.7 (m, 1 H), 1.7–1.95 (m, 3 H), 2.1–2.2 (m, 1 H), 2.3–2.35 (m, 2 H), 2.35–2.5 (m, 1 H), the NH signals were very broad]. The geometries of the semicarbazones were determined by proton homonuclear decoupling and ^{1}H NMR NOE experiments.

Selenium Dioxide Oxidation of Semicarbazones. A. General Procedure. The semicarbazone (0.1 mmol), selenium dioxide (22 mg, 0.2 mmol), and 1 mL of solvent were combined and stirred for 1–5 days. The reaction mixture was passed through filter aid, and the filter cake was washed well with methylene chloride or chloroform. The combined filtrate and washings were dried (K_2CO_3) and evaporated in vacuo at room temperature. The residue was examined directly by ^{1}H NMR or purified by preparative TLC with preservation of the original isomer composition and examined by NMR. The yields of crude organic products, which contained some TLC origin material, generally ranged between 50 and 100%; purification in several experiments indicated that around half the crude product was the desired selenadiazoles.

B. Example. Selenadiazoles 2a and 2b. A 1:9 Z/E mixture of semicarbazone 1 (2.18 g, 8.4 mmol) in 40 mL of anhydrous tetrahydrofuran was treated with selenium dioxide (1.85 g, 16.8 mmol) and stirred for 72 h under nitrogen. The reaction mixture was passed through Dicalite, and the cake was washed well with methylene chloride. Concentration of the filtrate and washings supplied a brown oil, which was triturated three times with hot ethyl acetate/hexane (1:6) and then with ethyl acetate. The supernatants were combined and evaporated in vacuo to give a mixture of selenadiazoles **2a** and **2b** as an orange oil (1.64 g, 66%). Flash chromatography with ethyl acetate/hexanes (gradient 1:6, 1:4, and 1:1) gave 0.78 g (32%) of pure **2a** as a yellow oil that solidified on standing [^{1}H NMR δ 1.85–1.9 (m, 2 H), 3.25–3.3 (m, 2 H), 3.50–3.55 (m, 2 H), 3.66 (s, 2 H), 4.15 (s, 2 H), 7.25–7.35 (m, 5 H)] and 0.38 g (16%) of pure **2b** as an orange oil [^{1}H NMR δ 2.79–2.82 (m, 2 H), 2.85–2.9 (m, 2 H), 3.20–3.22 (m, 2 H), 3.49–3.52 (m, 2 H), 3.77 (s, 2 H), 7.3–7.4 (m, 5 H)]. An analytical sample of **2a** was obtained by two recrystallizations from diethyl ether/hexanes as yellow plates, mp 77–78 °C. Anal. Calcd for $C_{13}H_{15}N_3Se$: C, 53.43; H, 5.17; N, 14.38. Found: C, 53.76; H, 4.95; N, 14.14.

Analytical Data for Selenadiazoles 7–9. The regioisomers of selenadiazoles **7–9** could not be separated by liquid chromatography or crystallization; hence, they were analyzed as mixtures.[20] **7a:7b** (purified as an oil; 40% yield): ^{1}H NMR (DMSO-d_6 at 77 °C) δ 1.12 (t, J = 7 Hz, 3 H, **7a**), 1.21 (t, J = 7 Hz, 2.3 H, **7b**), 1.8–1.95 (m, 2 H, **7a**), 3.26–3.28 (m, 1.53 H, **7b**), 3.35–3.45 (m, 2 H, **7a**), 3.45–3.55 (m, 1.53 H, **7b**), 3.6–3.75 (m, 6.6 H, **7a** and **7b**), 4.00 (q, J = 7 Hz, 2 H, **7a**), 4.10 (q, J = 7 Hz, 1.53 H, **7b**), 4.85 (s, 2 H, **7a**); HR-CI-MS (2-methylpropane) m/z calcd 276.0251, found 276.0230.

8a:8b (purified as off-white plates, 40% yield): mp 41–52 °C; ^{1}H NMR δ 2.03–2.08 (m, 2 H, **8a**), 2.8–2.85 (m, 0.33 H, **8b**), 3.08–3.11 (m, 2 H, **8a**), 3.50–3.53 (m, 2 H, **8a**), 3.55–3.58 (m, 0.33 H, **8b**), 3.63–3.66 (m, 0.33 H, **8b**), 3.85–3.88 (m, 0.33 H, **8b**), 4.11 (s, 2 H, **8a**). Anal. Calcd for $C_6H_8N_2SSe$: C, 32.88; H, 3.67; N, 12.78. Found: C, 33.25; H, 3.77; N, 12.70.[20]

9a:9b (purified as an oil, 42% yield): ^{1}H NMR δ 0.94 (s, 6 H, **9a**), 1.05 (s, 2.5 H, **9b**), 1.55–1.65 (m, 1.6 H, **9b**), 1.7–1.8 (m, 4 H, **9a**), 2.96 (s, 2 H, **9a**), 3.05–3.08 (m, 0.8 H, **9b**), 3.3–3.35 (m, 2.8 H, **9a** and **9b**); HR-CI-MS (2-methylpropane) m/z calcd 231.0399, found 231.0381.

Acknowledgment. We thank Dr. Allen B. Reitz for helpful advice and discussions, Dr. Gregory Leo for the ^{77}Se NMR spectral data, and Dr. David Burinsky for high-resolution CI mass spectral data. We are also indebted to Diane Gauthier, Dr. David Graden, and Dr. Leo for ^{1}H NMR spectral data.

Registry No. (*E*)-1, 134390-80-0; (*Z*)-1, 134390-79-7; **2a**, 134390-85-5; **2b**, 134390-86-6; **3**, 1208-76-0; (*E*)-**4**, 134418-63-6; **4** ketone, 56515-89-0; (*Z*)-**5**, 134390-81-1; **5** ketone, 22072-22-6; (*E*)-**6**, 134390-82-2; **6** ketone, 35099-49-1; **7a**, 134390-87-7; **7b**, 134390-88-8; **8a**, 134390-89-9; **8b**, 134390-90-2; **9a**, 134390-91-3; **9b**, 134390-92-4; (*E*)-**10**, 134390-96-8; (*Z*)-**10**, 134390-95-7; (*E*)-**11**, 134390-84-4; (*Z*)-**11**, 134390-83-3; **11** ketone, 134390-78-6; **12a**, 134390-93-5; **12b**, 134390-94-6.

(20) **Note added in proof:** Eventually, **8a** was obtained alone by recrystallizing the mixture of **8a:8b** from ether/hexane to give off-white platelets, mp 76–78 °C.

Notes

Selenium-Promoted Conversion of β-Diketones and β-Keto Esters into α,α-Dimethoxy β-Diketones and α,α-Dimethoxy β-Keto Esters

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We have recently reported that the reaction of diphenyl diselenide with ammonium peroxydisulfate produces phenylselenenyl sulfate, which acts as a strong phenylselenenylating agent for unsaturated compounds.[1] We have also observed that ammonium peroxydisulfate reacts with phenyl alkyl selenides to give the deselenenylation products, regenerating the phenylselenium electrophilic species. Thus, by use of an excess of ammonium peroxydisulfate and catalytic amounts of diphenyl diselenide, in a nucleophilic solvent like methanol, it was possible to effect in one pot the production of the phenylselenenylating agent, the alkoxyselenenylation of the unsaturated compounds, and the alkoxydeselenenylation of the addition products. This procedure has been used to effect useful conversions of alkenes into 1,1- and 1,2-dialkoxyalkanes,[2] methyl ketones into α-keto acetals,[3] and terminal and internal alkynes into α-keto acetals and α-keto ketals, re-

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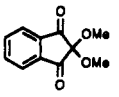
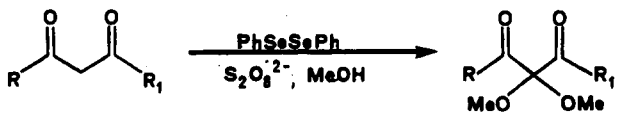
0022-3263/91/1956-5207$02.50/0

Table I. Conversion of β-Dicarbonyl Compounds 1 into Vicinal Monoprotected Tricarbonyl 2 and Diprotected Tetracarbonyl 3 Compounds[a]

	substrate	reaction time (h)		reaction products	yield[b] %
1a	$MeCOCH_2COMe$	1.5	2a	$MeCOC(OMe)_2COMe$	30[c]
1b	$MeCOCH_2COEt$	3	2b	$MeCOC(OMe)_2COEt$ +	45
			3b	$CH(OMe)_2COC(OMe)_2COEt$	15[c]
1c	$MeCOCH_2COPh$	3	2c	$MeCOC(OMe)_2COPh$ +	50
			3c	$CH(OMe)_2COC(OMe)_2COPh$	10[c]
1d	$PhCOCH_2COPh$	1	2d	$PhCOC(OMe)_2COPh$	70[d]
1e	$PhCOCH_2COEt$	1.5	2e	$PhCOC(OMe)_2COEt$	60
1f		1.5	2f		60
1g	$MeCOCH_2CO_2Me$	4	2g	$MeCOC(OMe)_2CO_2Me$ +	45
			3g	$CH(OMe)_2COC(OMe)_2CO_2Me$	27
1h	$MeCOCH_2CO_2CH_2Ph$	1.5	2h	$MeCOC(OMe)_2CO_2CH_2Ph$ +	45
			3h	$CH(OMe)_2COC(OMe)_2CO_2CH_2Ph$	15
1i	$EtCOCH_2CO_2Me$	1	2i	$EtCOC(OMe)_2CO_2Me$	60
1j	$n\text{-}PrCOCH_2CO_2Et$	1.5	2j	$n\text{-}PrCOC(OMe)_2CO_2Et$	75
1k	$PhCOCH_2CO_2Et$	1	2k	$PhCOC(OMe)_2CO_2Et$	70[e]

[a] The reactions were run in refluxing methanol. [b] Calculated on isolated products after column chromatography. [c] Other products were also present (see text). [d] A 10% yield of PhCOCOCOPh (6) was also isolated. [e] A 15% yield of $PhCOC(OH)_2CO_2Et$ (7) was also isolated.

Scheme I



1 2

R = alkyl, phenyl

R_1 = alkyl, phenyl, O-alkyl

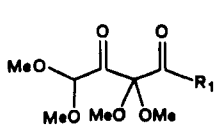
spectively.[4]

We now report that β-diketones and β-keto esters 1 also react with ammonium peroxydisulfate and diphenyl diselenide in methanol to afford the corresponding monoprotected vicinal tricarbonyl compounds 2 resulting from the conversion of the methylene into the $-C(OMe)_2-$ group (Scheme I). In the present case, however, the catalytic procedure described previously was not used, since a large excess of ammonium peroxydisulfate often resulted in the consumption of the starting β-dicarbonyl compounds and production of complex mixtures of products. Optimum results were obtained when diphenyl diselenide was used in stoichiometric amounts. This compound was then almost completely recovered at the end of the reaction. The results obtained with β-diketones **1a–f** and β-keto esters **1g–k** are summarized in Table I.

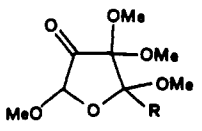
With the exception of acetylacetone (**1a**), from which **2a** was obtained in only 30% yield, all the other substrates afforded compounds **2** in moderate to good yields. A second reaction product was isolated in low yield from the reactions of the β-diketones **1b** and **1c** and the β-keto esters **1g** and **1h** that was identified as the diprotected vicinal tetracarbonyl derivative **3** (Table I). In the case of **1a**, compound **3a** could be detected by GLC–MS, but it could not be isolated. These results were not unexpected since all these substrates contain the MeCO moiety and we have previously observed that, under the same experimental conditions, methyl ketones are converted into the corresponding α-keto acetals.[3]

Experimental evidence for the formation of possible intermediates in the previous reaction could not be obtained. It can, however, be suggested that the conversion of compounds 1 into 2 takes place through a reaction sequence similar to that proposed for the conversion of methyl ketones into α-keto acetals.[3]

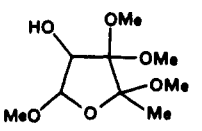
From β-diketones containing the MeCO group, **1a–c**, additional products were obtained. On the basis of spectral data, the cyclic structures **4** can be suggested for these compounds, indicating that they originate (like compound **3**) from the functionalization of the methyl group. Compound **4a** (7%) was isolated as a single stereoisomer, whereas compound **4c** (11%) was a 3:1 mixture of two stereoisomers that could not be separated. Finally, compound **4b** was detected by GLC–MS, but it could not be isolated in a pure form. In agreement with the proposed structure, reduction of **4a** with sodium borohydride, in THF at room temperature, afforded compound **5**; this was obtained as a single stereoisomer.



3b: R_1 = Et
3c: R_1 = Ph
3g: R_1 = OMe
3h: R_1 = OCH_2Ph



4a: R = Me
4b: R = Et
4c: R = Ph



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When the reaction mixtures derived from **1a–c**, **1g**, and **1h** were analyzed at the early stages (15 min), only unreacted starting materials and the corresponding monoprotected vicinal tricarbonyl compounds **2** were present. These results suggest that the reaction at the methylene occurs faster than that at the methyl group and the compounds **3** and **4** originate from **2**.

Vicinal tricarbonyl compounds have recently attracted a growing attention since they have been found in compounds possessing interesting properties[5] and find several practical[6] and synthetic applications.[7] The simple one-pot

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procedure described in this paper presents several advantages over other previously described methods for preparing vicinal triketones,[8] and it considerably extends the scope of substrates that undergo reaction with diphenyl diselenide and ammonium peroxydisulfate.

Experimental Section

Compound **1e**[9] was prepared as described in the literature. All the other starting compounds 1 were commercially available and were used without further purification. Reaction products were identified by proton and carbon-13 NMR spectroscopy, mass spectrometry, and elemental analyses.[3]

Conversion of β-Dicarbonyl Compounds into Vicinal Tricarbonyl Compounds. General Procedure. To a refluxing mixture of the β-dicarbonyl compound 1 (2 mmol) and diphenyl diselenide (1 mmol) in MeOH (10 mL) was added ammonium peroxydisulfate (4 mmol). The resulting mixture was stirred, and the progress of the reaction was monitored by TLC, GLC–MS, and NMR. The reaction mixture was poured into water and extracted with chloroform. The organic layer was washed with water, dried (Na_2SO_4), and evaporated. The reaction products were obtained in pure form after column chromatography on silica gel with mixtures of petroleum ether and ether (from 93:7 to 75:25) as eluants. Reaction times and yields are reported in Table I. Physical and spectral data of reaction products are reported in the following text.

3,3-Dimethoxy-2,4-pentanedione (2a): oil, ^{1}H NMR δ 3.25 (s, 6 H), 2.25 (s, 6 H); ^{13}C NMR δ 203.2, 105.6, 50.7, 26.4; MS *m/z* (relative intensity) 129 (8), 118 (11), 117 (94), 101 (3), 85 (17), 75 (66), 57 (17), 43 (100). Anal. Calcd for $C_7H_{12}O_4$: C, 52.50; H, 7.55. Found: C, 52.58; H, 7.47.

3,3-Dimethoxy-2,4-hexanedione (2b): oil, ^{1}H NMR δ 3.3 (s, 6 H), 2.65 (q, 2 H, J = 7.2 Hz), 2.3 (s, 3 H), 1.0 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 206.2, 203.8, 105.9, 50.8, 32.1, 26.6, 6.8; MS *m/z* (relative intensity) 143 (6), 131 (33), 117 (77), 103 (4), 85 (18), 75 (100), 57 (40), 43 (60). Anal. Calcd for $C_8H_{14}O_4$: C, 55.17; H, 8.10. Found: C, 55.24; H, 8.04.

1,1,3,3-Tetramethoxy-2,4-hexanedione (3b): oil, ^{1}H NMR δ 5.0 (s, 1 H), 3.45 (s, 6 H), 3.35 (s, 6 H), 2.6 (q, 2 H, J = 7.2 Hz), 1.0 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 203.4, 196.3, 103.5, 99.3, 54.7, 50.9, 31.7, 6.6; MS *m/z* (relative intensity) 203 (1), 177 (4), 146 (5), 131 (7), 85 (1), 75 (100), 57 (4), 47 (10). Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.28; H, 7.75. Found: C, 51.21; H, 7.68.

2,2-Dimethoxy-1-phenyl-1,3-butanedione (2c): oil; ^{1}H NMR δ 8.2–8.0 (m, 2 H), 7.7–7.2 (m, 3 H), 3.35 (s, 6 H), 2.2 (s, 3 H); ^{13}C NMR δ 202.2, 193.1, 134.1, 129.9, 128.9, 105.5, 50.9, 25.7; MS *m/z* (relative intensity) 222 (1), 179 (36), 151 (3), 135 (1), 117 (89), 105 (100), 77 (51), 75 (38), 43 (21). Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.86; H, 6.35. Found: C, 64.93; H, 6.44.

2,2,4,4-Tetramethoxy-1-phenyl-1,3-butanedione (3c): oil; ^{1}H NMR δ 8.2–8.0 (m, 2 H), 7.6–7.2 (m, 3 H), 4.95 (s, 1 H), 3.4 (s, 6 H), 3.2 (s, 6 H); ^{13}C NMR δ 196.0, 190.1, 133.3, 129.6, 128.3, 103.3, 99.2, 54.3, 51.0; MS *m/z* (relative intensity) 251 (1), 194 (3), 179 (11), 146 (6), 105 (20), 77 (12), 75 (100), 47 (7). Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43. Found: C, 59.66; H, 6.51.

2,2-Dimethoxy-1,3-diphenyl-1,3-propanedione (2d): mp 84–86 °C; ^{1}H NMR δ 8.25–8.0 (m, 2 H), 7.5–7.1 (m, 3 H), 3.4 (s, 3 H); ^{13}C NMR δ 192.5, 133.5, 129.5, 128.0, 103.9, 50.6; MS *m/z* (relative intensity) 284 (1), 253 (1), 179 (75), 151 (11), 105 (100), 77 (81). Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.74; H, 5.75.

1,3-Diphenyl-1,2,3-propanetrione (6): mp 76–78 °C (lit.[10] mp 70–71 °C); ^{1}H δ NMR 8.1–7.85 (m, 2 H), 7.7–7.3 (m, 3 H); ^{13}C NMR δ 194.4, 186.4, 134.8, 133.1, 129.9, 129.0; MS *m/z* (relative intensity) 210 (4), 105 (100), 77 (52).

2,2-Dimethoxy-1-phenyl-1,3-pentanedione (2e): oil; ^{1}H NMR δ 8.2–8.1 (m, 2 H), 7.6–7.3 (m, 3 H), 3.35 (s, 6 H), 2.55 (q, 2 H, J = 7.2 Hz), 0.95 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 205.1, 193.3, 134.2, 133.6, 130.0, 128.3, 105.6, 51.0, 31.5, 7.0; MS *m/z* (relative intensity) 205 (3), 179 (67), 151 (5), 131 (73), 105 (100), 75 (66), 51 (13). Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.01; H, 6.76.

2,2-Dimethoxy-1,3-indandione (2f): mp 69–71 °C (lit.[11] mp 70–71 °C); ^{1}H NMR δ 8.1–7.8 (m, 4 H), 3.7 (s, 6 H); ^{13}C NMR δ 192.8, 138.8, 136.3, 123.6, 90.3, 51.1; MS *m/z* (relative intensity) 206 (28), 163 (100), 147 (10), 135 (6), 133 (8), 105 (13), 104 (20), 77 (26), 76 (28), 50 (14).

Methyl 2,2-dimethoxy-3-oxobutanoate (2g): oil;[12] ^{1}H NMR δ 3.85 (s, 3 H), 3.4 (s, 6 H), 2.3 (s, 3 H); ^{13}C NMR δ 200.8, 165.4, 100.9, 52.2, 50.5, 25.6; MS *m/z* (relative intensity) 145 (4), 133 (100), 117 (16), 75 (18), 59 (44), 43 (39).

Methyl 2,2,4,4-tetramethoxy-3-oxobutanoate (3g): oil;[13] ^{1}H NMR δ 5.0 (s, 1 H), 3.8 (s, 3 H), 3.4 (s, 6 H), 3.35 (s, 6 H); ^{13}C NMR δ 194.0, 164.5, 99.3, 54.1, 52.0, 50.6; MS *m/z* (relative intensity) 205 (1), 177 (7), 133 (25), 105 (1), 75 (100), 59 (13), 47 (17).

Benzyl 2,2-dimethoxy-3-oxobutanoate (2h): oil; ^{1}H NMR δ 7.3 (s, 5 H), 5.25 (s, 2 H), 3.3 (s, 6 H), 2.2 (s, 3 H); ^{13}C NMR δ 200.9, 165.2, 134.5, 128.3, 128.1, 101.3, 67.4, 51.0, 25.9; MS *m/z* (relative intensity) 209 (47), 165 (1), 117 (8), 105 (24), 91 (100), 75 (7), 65 (8), 43 (14). Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.83; H, 6.46.

Benzyl 2,2,4,4-tetramethoxy-3-oxobutanoate (3h): oil; ^{1}H NMR δ 7.3 (s, 5 H), 5.25 (s, 2 H), 4.9 (s, 1 H), 3.3 (s, 6 H), 3.25 (s, 6 H); ^{13}C NMR δ 194.5, 164.4, 134.6, 128.6, 128.4, 99.7, 96.0, 67.6, 54.4, 51.3; MS *m/z* (relative intensity) 209 (5), 177 (1), 133 (2), 91 (31), 75 (100), 59 (1), 47 (4). Anal. Calcd for $C_{15}H_{20}O_7$: C, 57.69; H, 6.46. Found: C, 57.60; H, 6.50.

Methyl 2,2-dimethoxy-3-oxopentanoate (2i): oil; ^{1}H NMR δ 3.8 (s, 3 H), 3.3 (s, 6 H), 2.7 (q, 2 H, J = 7.0 Hz) 1.1 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 204.1, 166.2, 101.6, 52.7, 51.5, 31.7, 7.0; MS *m/z* (relative intensity) 159 (2), 133 (100), 75 (15), 59 (25), 57 (8), 47 (3). Anal. Calcd for $C_8H_{14}O_5$: C, 50.53; H, 7.42. Found: C, 50.46; H, 7.50.

Ethyl 2,2-dimethoxy-3-oxohexanoate (2j): oil; ^{1}H NMR δ 4.3 (q, 2 H, J = 7.2 Hz), 3.3 (s, 6 H), 2.65 (t, 2 H, J = 7.2 Hz), 1.65 (sext, 2 H, J = 7.2 Hz), 1.3 (t, 3 H, J = 7.2 Hz), 0.9 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 203.1, 165.4, 101.4, 61.8, 50.8, 40.0, 16.2, 13.7, 13.2; MS *m/z* (relative intensity) 187 (1), 148 (8), 147 (100), 119 (20), 85 (2), 75 (15), 59 (28), 47 (30). Anal. Calcd for $C_{10}H_{18}O_5$: C, 55.04; H, 8.31. Found: C, 55.11: H, 8.37.

Ethyl 2,2-dimethoxy-3-phenyl-3-oxopropanoate (2k): oil; ^{1}H NMR δ 8.25–8.15 (m, 2 H), 7.7–7.4 (m, 3 H), 4.25 (q, 2 H, J = 7.1 Hz), 3,45 (s, 6 H), 1.1 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 190.1, 165.7, 133.5, 133.2, 128.9, 128.1, 100.4, 61.7, 50.7, 13.3; MS *m/z* (relative intensity) 221 (1), 179 (14), 147 (100), 119 (19), 105 (42), 77 (33), 47 (28). Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.82; H, 6.45.

Ethyl 2,2-dihydroxy-3-phenyl-3-oxopropanoate (7): oil; ^{1}H NMR δ 8.15–8.05 (m, 2 H), 7.7–7.4 (m, 3 H), 4.95 (br s, 2 H), 4.2 (q, 2 H, J = 7.1 Hz), 1.1 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 191.6, 169.8, 135.4, 134.5, 130.1, 129.4, 91.7, 63.1, 13.5; MS *m/z* (relative intensity) 178 (1), 150 (1), 105 (100), 77 (35), 51 (9). Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.39. Found: C, 59.01; H, 5.30.

2,4,4,5-Tetramethoxy-5-methyltetrahydrofuran-3-one (4a): oil; ^{1}H NMR δ 4.9 (s, 1 H), 3.55 (s, 3 H), 3.45 (s, 3 H), 3.4 (s, 3 H), 3.3 (s, 3 H), 1.6 (s, 3 H): ^{13}C NMR δ 200.8, 105.6, 98.3, 97.4, 56.9, 50.9, 50.8, 49.0, 17.2; MS *m/z* (relative intensity) 189 (9), 161 (9), 146 (38), 132 (21), 131 (16), 117 (71), 85 (26), 75 (100),

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59 (11), 57 (28), 43 (52). Anal. Calcd for $C_9H_{16}O_6$: C, 49.09; H, 7.32. Found: C, 49.15; H, 7.21.

2,4,4,5-Tetramethoxy-3-hydroxy-5-methyltetrahydrofuran (5): oil; ^{1}H NMR δ 4.93 (d, 1 H, J = 5.2 Hz), 4.04 (dd, 1 H, J = 5.2 and 10.5 Hz), 3.54 (s, 3 H), 3.43 (s, 3 H), 3.35 (s, 3 H), 3.3 (s, 3 H), 3.05 (d, OH, J = 10.5 Hz), 1.4 (s, 3 H); ^{13}C NMR δ 106.6, 104.9, 102.5, 72.2, 56.4, 51.0, 49.7, 48.6, 17.6; MS m/z (relative intensity) 191 (1), 145 (11), 131 (100), 117 (53), 85 (16), 75 (44), 59 (13), 57 (7), 43 (26). Anal. Calcd for $C_9H_{18}O_6$: C, 48.65; H, 8.16. Found: C, 48.58; H, 8.21.

2,4,4,5-Tetramethoxy-5-phenyltetrahydrofuran-3-one (4c): oil; ^{1}H NMR δ 7.7–7.55 (m, 2 H), 7.5–7.3 (m, 3 H), 5.15 (s, 1 H), 3.6 (s, 3 H), 3.4 (s, 3 H), 3.3 (s, 3 H), 3.1 (s, 3 H); MS m/z (relative intensity) 251 (4), 194 (3), 179 (27), 146 (100), 131 (28), 117 (34), 105 (59), 77 (39), 75 (43), 59 (12). A second isomer could be detected by ^{1}H NMR and GLC–MS: ^{1}H NMR δ 7.7–7.55 (m, 2 H), 7.5–7.3 (m, 3 H), 4.9 (s, 1 H), 3.65 (s, 3 H), 3.38 (s, 3 H), 3.28 (s, 3 H), 3.15 (s, 3 H); MS m/z (relative intensity) 251 (2), 194 (3), 179 (35), 146 (100), 131 (29), 117 (33), 105 (56), 77 (36), 75 (41), 59 (10). Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43. Found: C, 59.71; H, 6.32.

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Registry No. **1a**, 123-54-6; **1b**, 3002-24-2; **1c**, 93-91-4; **1d**, 120-46-7; **1e**, 5331-64-6; **1f**, 606-23-5; **1g**, 105-45-3; **1h**, 5396-89-4; **1i**, 30414-53-0; **1j**, 3249-68-1; **1k**, 94-02-0; **2a**, 134390-33-3; **2b**, 134390-34-4; **2c**, 134390-35-5; **2d**, 134390-36-6; **2e**, 134390-37-7; **2f**, 65299-21-0; **2g**, 68057-56-7; **2h**, 134390-38-8; **2i**, 134390-39-9; **2j**, 134390-40-2; **2k**, 134390-41-3; **3a**, 134390-49-1; **3b**, 134390-42-4; **3c**, 134390-43-5; **3g**, 90690-66-7; **3h**, 134390-44-6; **4a**, 134390-46-8; **4b**, 134390-51-5; **4c** (isomer 1), 134390-48-0; **4c** (isomer 2), 134390-50-4; **5**, 134390-47-9; **6**, 643-75-4; **7**, 134390-45-7; PhSeSePh, 1666-13-3; ammonium peroxydisulfate, 7727-54-0.

Substituted γ-Lactones: Reactions of (Arylmethylene)furandiones with Nucleophiles. A Novel Approach to the Cyclolignan Lactone Skeleton[1]

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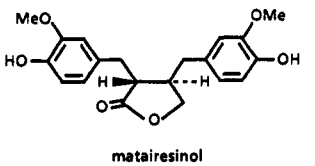
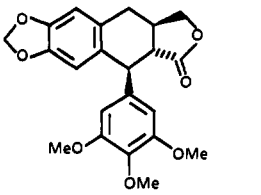
Introduction

In the field of cancer research, an important class of natural products derived formally from the dimerization of 3-phenylpropane precursors,[3] namely, lignan lactones, is well recognized.[4] The many varied types of structures that lignan lactones can possess, e.g., **1–3**, ..., etc., have presented a considerable challenge to organic chemists over the years and indeed many elegant syntheses for their skeleton have been reported.[5,6]



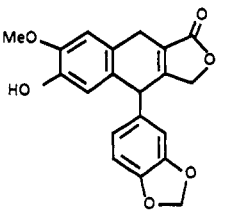
matairesinol

1



(-)-isodeoxypodophyllotoxin

2



Konyanin

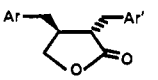
3

Of particular interest to us are type 1 compounds for which we devised the first synthesis of their unsymmetrical analogues **4**.[7]

In the continuation of studies of the chemistry of β- and α-tetronic acids **5** and **6**, we wish to report our finding in utilizing these molecules in building up the lignan lactone skeleton.

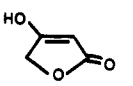
Results and Discussion

Retrosynthetically, the construction of **4** can be approached in a convergent manner and would involve a

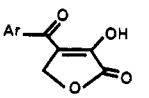


4

Horner–Emmons reaction of a phosphonate carbanion such as the anion derived of diethyl benzylphosphonate (**9**) with the ketonic group of either **7** or **8** (formally obtained from **5** or **6** respectively)[8,9] followed by a hydrogenation of the double bonds and epimerization by base at C-3.



5



6

A Horner–Emmons reaction of **7** with **9**, however, failed to produce the desired 1,2-adduct. Instead **7** reacted as a Michael acceptor yielded compounds of type **10**. Their structural assignments were based on elemental analysis and spectroscopic data (Scheme I).

The existence of several studies concerning the factors governing the reactivity of stabilized carbanions such as **9** with α,β-unsaturated carbonyl compounds as to 1,2- versus 1,4-addition, e.g., Horner–Emmons fashion or Michael addition,[10,11] prompted us to apply a number of

(1) This is part 37 of the series Substituted γ-Butyrolactones. For part 36 of this series, see: Zimmer, H.; Amer, A.; Chiem Van Pham; Schmidt, D. S. *J. Org. Chem.* **1988**, *53*, 3368.

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