N,N'-Dimethyl-5-hydroxy-5-(1,1,3-triphenylpropyl)hydantoin (23): mp 192–195 °C dec; IR ($CHCl_3$) 3300, 1770, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.6–1.8 (m, 1 H), 2.0–2.8 (m, 2 H), 2.19 (s, 3 H, NMe), 2.57 (s, 3 H, NMe), 3.3–3.5 (m, 1 H), 4.77 (br s, 1 H, OH), 6.9–7.4 (m, 13 H, Ph), 7.6–7.8 (m, 2 H, Ph); ^{13}C NMR δ 23.8 (q), 27.7 (q), 30.4 (t), 35.4 (t), 58.7 (s), 91.7 (s), 125.7 (d), 127.1 (d), 127.7 (d), 128.2 (d), 130.2 (d), 130.7 (d), 136.5 (s), 141.1 (s), 142.3 (s), 155.6 (s), 172.9 (s). Anal. Calcd for $C_{26}H_{26}N_2O_3$: C, 75.34; H, 6.32; N, 6.76. Found: C, 75.02; H, 6.38; N, 6.68.

N,N'-Dimethyl-5-hydroxy-5-(2-cyclohexyl-1,1-diphenylethyl)hydantoin (25): mp 202–203 °C dec; IR ($CHCl_3$) 3300, 1770, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.3–1.7 (m, 11 H, cyclohexyl), 2.0–2.3 (m, 1 H, CH_2), 2.23 (s, 3 H, NMe), 2.66 (s, 3 H, NMe), 3.01 (br d, 1 H, J = 14.7 Hz, CH_2), 4.77 (s, 1 H, OH), 7.2–7.3 (m, 8 H, Ph), 7.6–7.8 (m, 2 H, Ph); ^{13}C NMR δ 23.9 (q), 26.2 (t), 26.8 (t), 28.1 (q), 34.0 (d), 34.5 (t), 35.8 (t), 40.2 (t), 59.7 (s), 91.9 (s), 127.0 (d), 127.4 (d), 130.5 (d), 130.8 (d), 137.8 (s), 141.7 (s), 155.6 (s), 173.1 (s). Anal. Calcd for $C_{25}H_{30}N_2O_3$: C, 73.86; H, 7.44; N, 6.89. Found: C, 73.79; H, 7.54; N, 6.77.

N,N'-Dimethyl-5-hydroxy-5-benzylhydantoin (24), N,N'-dimethyl-5-hydroxy-5-cyclohexylhydantoin (26), and N,N'-dimethyl-5-hydroxy-5-(hydroxymethyl)hydantoin (27) were identified by direct comparison with authentic samples.[6]

N,N'-Dimethyl-5-hydroxy-5-(4-methoxy-1,1,4,4-tetramethyl-2-butenyl)hydantoin (28) was a mixture of *E* and *Z* isomers. The major *E* isomer was isolated by recrystallization: mp 89–90 °C; IR ($CHCl_3$) 3350, 1770, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (s, 3 H), 1.22 (s, 3 H), 1.25 (s, 3 H × 2), 2.92 (s, 3 H, NMe), 2.96 (3 H, NMe), 3.12 (s, 3 H, OMe), 4.43 (s, 1 H, OH), 5.48 (AB q, 1 H, J = 16.4 Hz, CH=), 5.85 (AB q, 1 H, J = 16.4 Hz, =CH); ^{13}C NMR δ 21.5 (q), 23.1 (q), 24.4 (q), 25.4 (q), 26.0 (q), 27.6 (q), 43.8 (s), 50.2 (q), 74.9 (s), 89.6 (s), 133.2 (d), 135.4 (d), 156.6 (s), 173.5 (s). Anal. Calcd for $C_{14}H_{24}N_2O_4$: C, 59.13; H, 8.50; N, 9.85. Found: C, 59.03; H, 8.63; N, 9.77. The minor *Z* isomer could not be purified: characteristic signals ^{13}C NMR ($CDCl_3$) δ 50.1 (s, OMe), 131.8 (d, CH=), 137.5 (d, CH=).

N,N'-Dimethyl-5-hydroxy-5-(5-hydroxy-2-pentenyl)hydantoin (29) was a mixture of *E* and *Z* isomers: bp 80 °C (10^{-3} Torr); IR ($CHCl_3$) 3400, 1780, 1720 cm^{-1}; characteristic signals ^1H NMR ($CDCl_3$) δ 2.0–2.4 (m), 2.60 (t, J = 6.1 Hz), 2.90 (s), 2.95 (s), 3.4–3.6 (m), 5.1–5.7 (m), 5.86 (br s); ^{13}C NMR δ 24.0 (q), 24.5 (q), 35.6 (t), 37.3 (t), 61.6 (t), 86.5 (s), 123.3 (d), 133.4 (d), 155.7 (s), 173.6 (s); weak signals at δ 86.4 (s), 122.2 (d), 131.7 (d). Anal. Calcd for $C_{10}H_{16}N_2O_4$: C, 52.62; H, 7.07; N, 12.27. Found (for a mixture of the isomers): C, 52.40; H, 7.03; N, 11.98. **N,N'-Dimethyl-5-hydroxy-5-(3-hydroxy-1-vinylpropyl)hydantoin** (a 1,2-adduct) was separated from **29** by chromatography but could not be completely purified and did not give satisfactory analytical data: characteristic signals ^{13}C NMR ($CDCl_3$) δ 23.9 (q), 24.4 (q), 24.6 (q), 25.0 (q), 30.4 (t), 30.6 (t), 46.2 (d), 59.8 (t), 60.5 (t), 86.5 (s), 87.1 (s), 120.1 (t), 120.9 (t), 134.1 (d), 134.3 (d), 155.6 (s), 156.2 (s), 173.0 (s), 173.6 (s).

(E)-N,N'-Dimethyl-5-hydroxy-5-(5-phenyl-2-pentenyl)hydantoin (30): bp 130 °C (10^{-3} Torr); IR ($CHCl_3$) 3350, 1780, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.30 (t, 2 H, J = 7.3 Hz), 2.5–2.7 (m, 4 H), 2.86 (s, 3 H, NMe), 2.92 (s, 3 H, NMe), 4.85 (br s, 1 H, OH), 4.9–5.8 (m, 2 H), 7.1–7.4 (m, 5 H); ^{13}C NMR δ 24.0 (q), 24.5 (q), 34.1 (t), 35.5 (t), 37.2 (t), 86.5 (s), 120.7 (d), 125.9 (d), 128.3 (d), 136.8 (d), 141.3 (s), 155.5 (s), 173.6 (s). Anal. Calcd for $C_{16}H_{20}N_2O_3$: C, 66.65; H, 6.99; N, 9.72. Found: C, 66.57; H, 7.25; N, 9.40.

(E)- and (Z)-N,N'-dimethyl-5-hydroxy-5-(4-cyclohexyl-2-butenyl)hydantoin (31) and N,N'-dimethyl-5-hydroxy-5-(2-cyclohexyl-1-vinylethyl)hydantoin (32) could not be separated: bp 110 °C (10^{-3} Torr); IR ($CHCl_3$) 3350, 1780, 1710 cm^{-1}; characteristic signals ^{13}C NMR ($CDCl_3$) δ 24.0 (q), 24.5 (q), 37.1 (t), 40.4 (t), 86.7 (s), 120.9 (d), 136.6 (d), 155.5 (s), 173.6 (s); weak signals at 46.8 (d), 46.9 (d), 121.0 (t), 121.2 (t), 134.7 (d), 135.4 (d). Anal. Calcd for $C_{15}H_{24}N_2O_3$: C, 64.26; H, 8.63; N, 9.99. Found (for a mixture of the isomers): C, 64.44; H, 8.95; N, 9.75.

Quantum Yield Determination. Valerophenone actinometry[23] was used. Irradiation was performed with a 300-W high-pressure mercury lamp in a merry-go-round apparatus. The 313-nm line was isolated with a filter solution containing 0.002 M potassium chromate in 5% aqueous potassium carbonate. The sample in a Pyrex tube was degassed to ca. 10^{-3} Torr in three freeze–thaw cycles. After irradiation, the degree of reaction (consumption of **1**) was determined by gas chromatography.

Registry No. **1**, 5176-82-9; **2**, 530-48-3; **3**, 119695-55-5; **4**, 103-30-0; **5**, 119846-69-4; **6**, 563-79-1; **7**, 119695-56-6; **8**, 119695-57-7; **9**, 119695-58-8; **10**, 164-13-6; **11** (isomer 1), 119695-59-9; **11** (isomer 2), 119695-75-9; **12**, 106-99-0; **13** (isomer 1), 119695-60-2; **13** (isomer 2), 119695-76-0; **14**, 119695-61-3; **15**, 119695-62-4; **16**, 119695-63-5; **18**, 119695-64-6; **19**, 119695-65-7; **20**, 119695-66-8; **21**, 119695-67-9; **22**, 64732-10-1; **23**, 119695-68-0; **24**, 98619-34-2; **25**, 119695-69-1; **26**, 98619-36-4; **27**, 98619-35-3; **28** (isomer 1), 119695-70-4; **28** (isomer 2), 119695-77-1; **29** (isomer 1), 119695-71-5; **29** (isomer 2), 119695-78-2; **30**, 119695-72-6; **31** (isomer 1), 119695-73-7; **31** (isomer 2), 119695-80-6; **32**, 119695-74-8; ethyl vinyl ether, 109-92-2; acrylonitrile, 107-13-1; *N,N'*-dimethyl-5-hydroxy-5-(3-hydroxy-1-vinylpropyl)hydantoin, 119695-79-3.

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Studies toward the Syntheses of Functionally Substituted γ-Butyrolactones and Spiro-γ-butyrolactones and Their Reaction with Strong Acids: A Novel Route to α-Pyrones

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A general strategy for the conversion of 5-keto carboxylic acids, **6** (via their enol–lactones **7**), to a variety of γ-lactones, **8a–c**, and spiro-γ-lactones, **8d–g**, is described. Lactones **8b** and **8d,e** may be further converted into the corresponding α-pyrones, **17b** and **17d,e**, respectively, in the presence of strong acids.

The synthesis of γ-lactones and spiro-γ-lactones has been the focus of recent interest thanks to their presence in a large number of natural products.[1] Of particular importance, however, is the preparation of functionalized

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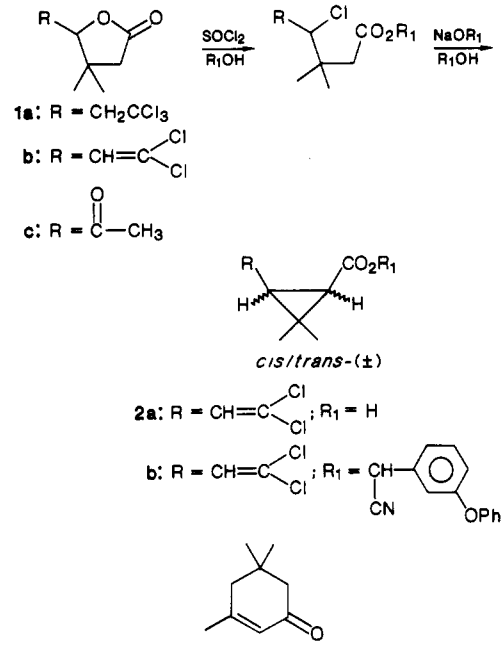
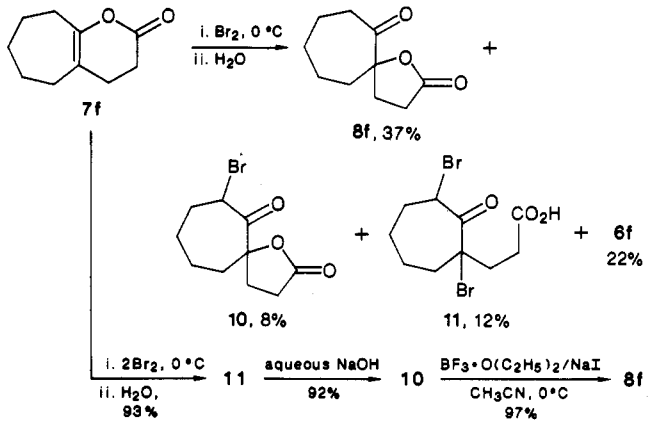
γ-lactones,[2] whose potential as synthons in natural product synthesis is well documented.[2a,3] In addition, γ-lactones of the type 1 hold special interest[4] in view of their utility as precursors to the cyclopropanecarboxylic acid esters, 2,[5] related to a potential class of insecticides, synthetic pyrethroids.

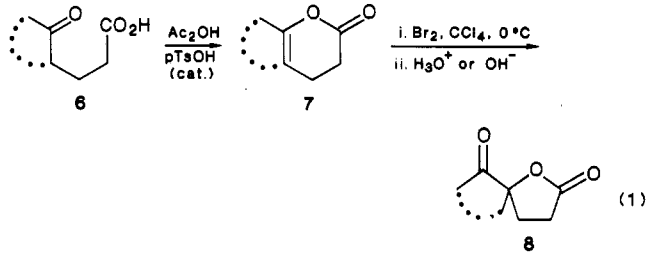


Our interest in synthetic pyrethroids[6] led us to develop new approaches to the preparation of functionally substituted γ-lactones, based on inexpensive and readily available raw materials. Accordingly, we reported recently

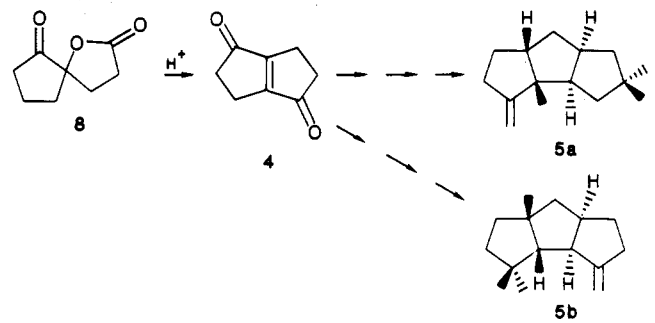
Scheme I



an expeditious synthesis of **1c**, from isophorone, **3**, which was further elaborated to the *cis*-/*trans*-(±)-**2a**,[7] an important intermediate in the production of **2b**. We have also communicated a methodology for the preparation of a few functionally substituted γ-lactones and spiro-γ-lactones, **8**, from the corresponding 5-keto carboxylic acids, **6**, via their enol–lactones, **7** (eq 1). As an extension of this



work, we disclose in this paper a general synthesis of **8** based on the above reaction. The reaction of **8** with strong acids was also studied with a view toward the synthesis of **4**, possible synthon for the triquinane natural products, (±)-hirsutene, **5a**, and (±)-capnellene, **5b**. Such a reaction



might be expected in view of the earlier results obtained with γ-lactones.[9] To our surprise, however, the above

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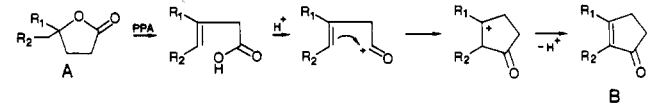
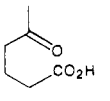
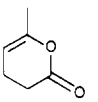
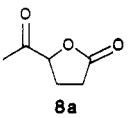
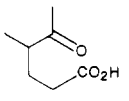
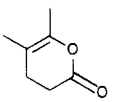
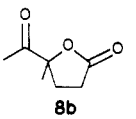
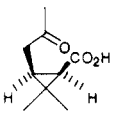
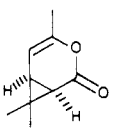
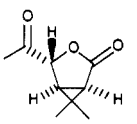
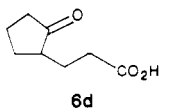
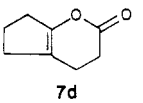
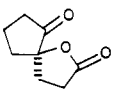
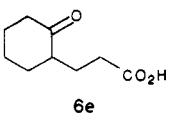
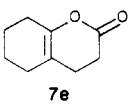
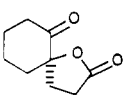
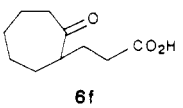
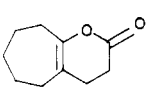
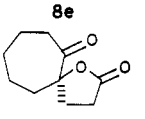
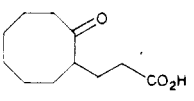
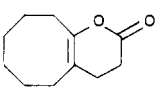
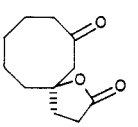


Eaton, P. E.; Mueller, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 1014. Jacobson, R. M.; Clader, J. W. *Tetrahedron Lett.* **1980**, 1205. Guzman, A.; Mendoza, S. *Synthesis* **1981**, 989. Rai, C.; Dev. S. *J. Ind. Chem. Soc.* **1957**, *34*, 178.

Table I. Syntheses of γ,δ-Enol-Lactones, 7 and γ-Lactones and Spiro-γ-lactones, 8

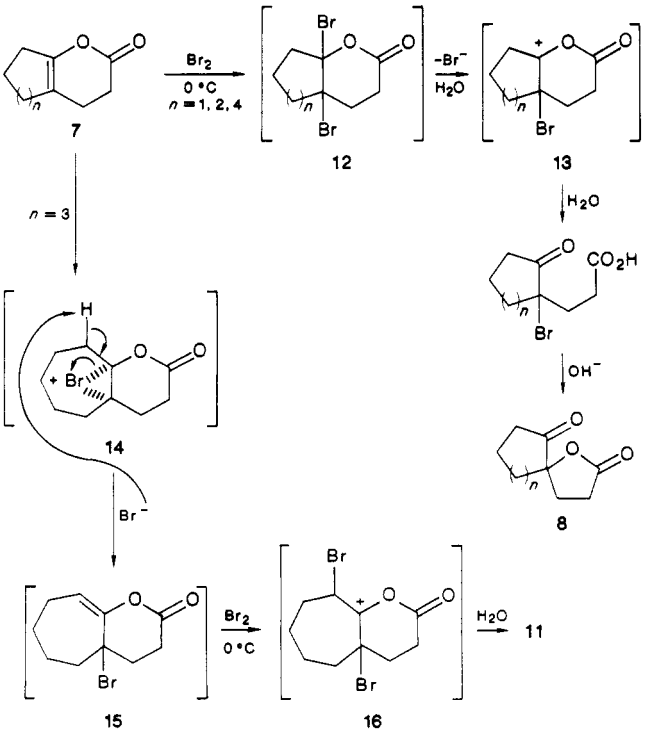
entry	acid	γ,δ-enol-lactones, 7	yield,[a] %	γ-lactones 8	yield,[a] %
1	 6a	 7a	83	 8a	80
2	 6b	 7b	81	 8b	73
3	 (-)-6c	 (-)-7c	85	 (+)-8c	98
4	 6d	 7d	80	 8d	79
5	 6e	 7e	80	 8e	80
6	 6f	 7f	82	 8f	83[b]
7	 6g	 7g	84	 8g	78[c]

[a] Isolated yield of pure products by distillation or crystallization. [b] Overall yield of three steps (Scheme II). [c] Overall yield of two steps (eq 5).

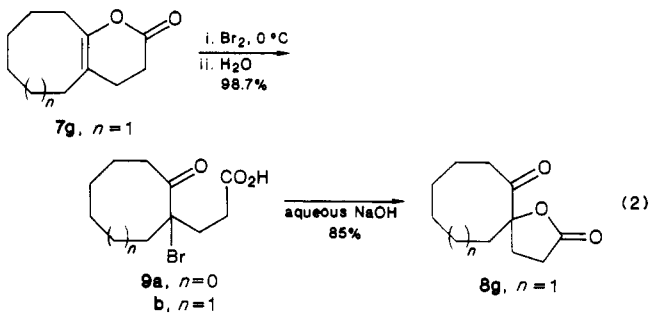
reaction yielded the substituted α-pyrone derivatives, **17**, instead.

Synthesis of γ-Lactones and Spiro-γ-lactones, 8. The enol-lactones **7a–g** required for this study were prepared, in excellent yields, from the corresponding 5-keto carboxylic acid derivatives, **6**,[10] through standard procedures (Table I).[11] The reactions of **7** with bromine (1:1) were carried out at 0 °C, and the resultant intermediates were hydrolyzed (1:1 tettrahydrofuran–water or saturated aqueous sodium bicarbonate) to yield the desired lactones, **8**. The results are summarized in Table I. Thus, **7a–e** yielded the γ-lactones, **8a–c**, and spiro-γ-lactones, **8d,e**, in excellent yields (entries 1–5, Table I), while **7g** furnished the uncyclized product, **9b**, instead, in quantitative yield. However, upon treatment with a stronger base (0.3 M aqueous sodium hydroxide), **9b** was smoothly converted to the desired spiro-γ-lactone, **8g**, in high yield (eq 2). In contrast, the reaction of **7f** afforded a mixture of products, the desired spiro-γ-lactone, **8f**, being formed in only 37% yield (Scheme I). It is difficult to rationalize the unusually large proportions of halogenated products (**10** and **11**) in the above reaction with **7f**, given that their formation was not observed with **7d,e** or with **7g**. This difference in

Scheme II



(10) 5-Keto carboxylic acids, **6d–f**, were prepared from the corresponding ketones, via alkylation of the enamines with methyl acrylate, followed by hydrolysis. Stork, G.; et al. *J. Am. Chem. Soc.* **1963**, *85*, 207.
(11) Roman, S. A. U.S. Patent 1979, 4156692.

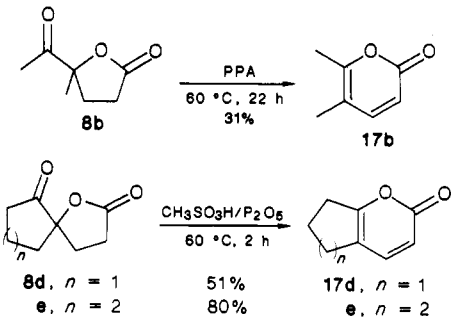


reactivities between **7f** and the other enol-lactones is further accentuated in reaction employing 2 equiv of bromine; thus, while **7f** rapidly consumed all the bromine to yield the dihalogenated product **11** as the sole product at 0 °C, **7d,e** and **7g** failed to react with excess bromine and continued to produce the corresponding spiro-γ-lactones, **8d,e** and **8g** as the sole products, under the same conditions.

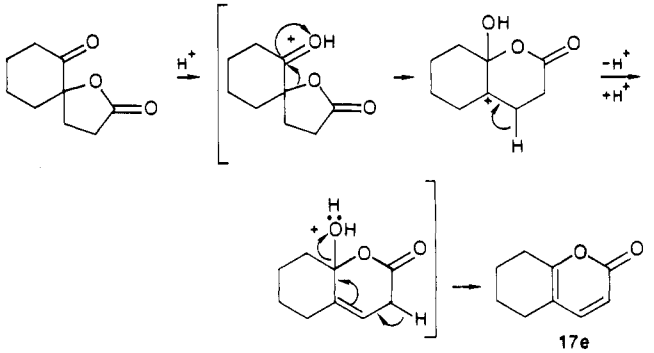
Scheme II is proposed to account for our results. The mechanism recognizes the intermediacy of the bromide adduct, **12**, and its solvolysis via the resonance-stabilized carbonium ion **13** (with some bromonium ion character). Subsequent reaction of **13** with water yielded 4-bromo carboxylic acid derivatives, which when treated with base yielded the γ-lactones **8a–e** and **8g**. We infer that in the case of **7f** the olefin (**15**) formation pathway is facilitated by stereoelectronic factors, e.g. the antiperiplanar configuration of the C–H and C–Br^+ bonds in **14**, favoring elimination.[12] Further bromination of **15** to **16** followed by its hydrolysis would yield the dibromo keto carboxylic acid, **11**.

The conversion of **11** to the γ-lactone, **10**, could be effected, as before, in excellent yield, with aqueous sodium hydroxide solution. The position of bromine in **10** was confirmed from (i) spectral data (^{1}H NMR δ 4.44 (*dd*, *J* = 13.2 Hz, 5.1 Hz); ^{13}C NMR δ (49.14)) and (ii) by the ready dehalogenation of **10** to **8f** with a combination of boron trifluoride etherate and sodium iodide in acetonitrile.[13] It was thus possible to obtain **8f** in high yield from **7f**, albeit in three steps. Finally, the above bromolactonization reaction was also found to be stereoselective, yielding exclusively (+)-**8c** from (−)-**7c** (entry 3, Table I).

Reaction of 8 with Strong Acids. The reaction of **8f** with a combination of methanesulfonic acid and phosphorus pentoxide (25:1) was carried out at 60 °C.[9] While **8a** and **8g** underwent extensive polymerization, **8d** and **8e** yielded the corresponding α-pyrones **17d** and **17e** in yields of 50% and 80%, respectively. Compounds **8b** and **8f**, however, remained unreacted, and forcing condition resulted in a gradual undesired polymerization. Consequently, **8b** and **8f** were reacted with freshly prepared polyphosphoric acid (PPA), and while no reaction was observed with **8f**, **8b** yielded the corresponding α-pyrone, **17b**, in ~31% yield.



We postulate the following mechanism to explain the formation of the above α-pyrone derivatives. While our initial objective of converting **8** to the intermediate **4** with strong acid could not be achieved, the formation of the α-pyrones **17** is nevertheless rewarding in view of their potential as dienes in Diels–Alder reactions.[14]



In conclusion, we have demonstrated a facile general route for the preparation of functionalized γ-lactones and spiro-γ-lactones, **8**, from the corresponding 5-keto carboxylic acids, **6**, via their γ,δ-enol-lactones, **7**. The above reaction may be achieved in a single step with **7a–e** and via isolable bromocarboxylic acid derivatives in the case of **7f–g**. The reaction of some of these compounds with strong acids also yielded the α-pyrone ring system.

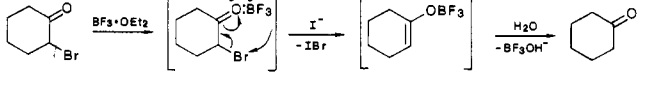
Experimental Section

Melting points and boiling points were uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ on Bruker CW-80 and Bruker AC-80 spectrometers with chemical shifts expressed as δ units with Me_4Si as internal standard. ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker A-80 spectrometer with chemical shifts expressed as δ units with Me_4Si as the internal standard. IR spectra were recorded in $CHCl_3$ on a Perkin-Elmer 781 spectrophotometer; absorptions are reported in wave numbers (cm^{-1}). GC–MS were recorded on a Hewlett-Packard 5993 B spectrometer using 2% OV-210 on Chromosorb WHP 80/100, 2 m × 0.6 cm column (column C). GLC analyses were carried out on a Pye-Unicam 204 gas chromatograph using 3% OV-17 on a diatomaceous earth Q, 100/120, 6 ft × $^1/_4$ in. column (column A) and capillary column HP 101 (methyl silicone), 25 m × 0.2 mm × 0.2 μm film thickness (column B). 4-Acetylbutyric acid, **6a**, was purchased from Aldrich Co., while **6b** was prepared via the alkylation of **6a** with methyl iodide in the presence of sodium hydride. Compounds (−)-**6c**[6] and **6d–g**[10] were prepared via literature procedures.

General Procedure for the Synthesis of Enol-Lactones, 7. A mixture of keto acid, **6** (0.17 mol), acetic anhydride (65 mL, 0.68 mol), *p*-toluenesulfonic acid dihydrate (3.6 g, 17 mmol), and benzene (150 mL) was stirred at 0 °C for 2–4 h until all the acid disappeared (TLC). The dark brown reaction mixture was diluted

(12) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: New York, 1983; Vol. 1, pp 254–255. We thank one of the referees for suggesting this possibility to us.

(13) A number of 2-bromo ketones can be dehalogenated with a combination of boron trifluoride etherate and iodide ion. Mandal, A. K.; Mahajan, S. W., unpublished observations.



For other uses of this reagent, see: Mandal, A. K.; et al. *Synthesis* **1985**, 274; **1986**, 221. *Tetrahedron Lett.* **1985**, 3863. *Tetrahedron*, in press.

(14) (a) Shusherina, N. P. *Russ. Chem. Rev. (Engl. Transl.)* **1974**, *43*, 851. For recent reactions: (b) Boger, D. L.; Mullican, *Tetrahedron Lett.* **1983**, *24*, 4939; **1982**, *23*, 4551. (c) Cano, P.; Echavarren, A.; Pradoo, P.; Farina, F. *J. Org. Chem.* **1983**, *48*, 5373. (d) Tamura, Y.; Mohri, S.; Maeda, H.; Tsugoshi, H.; Kita, Y. *J. Org. Chem.* **1982**, *47*, 4376.

with ether (200 mL). The reaction mixture was washed successively with aqueous saturated sodium bicarbonate solution (3 × 200 mL) and saturated aqueous brine solution (50 mL). The organic layer was dried over anhydrous sodium sulfate and filtered, and the solvent was removed under aspirator vacuum. Distillation under reduced pressure provided pure **7**.

7a: bp 78–80 °C (3 mm) [lit.[15] bp 82–3 °C (3 mm)]; 96% (column A); IR 1750, 1700 cm^{-1}; ^1H NMR δ 1.9 (s, 3 H, CH_3C=C), 2.1–2.4 (m, 2 H, CH_2), 2.4–2.7 (m, 2 H, CH_2C=O), 5.0 (t, 1 H, CH=).

7b:[16] bp 66–8 °C (1 mm); 95% (column B); IR 1750, 1700 cm^{-1}; ^1H NMR δ 1.7 (s, 3 H, CH_3), 1.9 (s, 3 H, CH_3C=), 2.05–2.35 (m, 2 H, CH_2), 2.4–2.7 (m, 2 H, CH_2C=O); ^{13}C NMR δ 212.74, 177.96, 46.14, 31.55, 28.15, 27.33, 16.22.

7c: bp 68–70 °C (0.5 mm); mp 48 °C (lit.[11] mp 44–45.5 °C); 100% (column B); $[\alpha]^{25}_D$ −100° (C1, $CHCl_3$); IR 1745, 1720 cm^{-1}; ^1H NMR δ 1.02 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 1.6–1.8 (m, 2 H, bridge), 1.88 (m, 3 H, CH_3C=), 5.0–5.15 (m, 1 H, CH=).

7d: bp 90–1 °C (2 mm); 96.3% (column A); further purification by column chromatography (eluent, *n*-hexane) followed by bulb-to-bulb (Kugelrohr) distillation (oven temperature 90 °C (1 mm)) yielded an analytical sample, 99.3%; IR 1765, 1715, 1665 cm^{-1}; ^1H NMR δ 1.75–2.8 (m, 10 H, 5 CH_2). Anal. Calcd for $C_8H_{10}O_2$: C, 69.57; H, 7.25. Found: C, 69.40; H, 7.18.

7e: bp 95–98 °C (2 mm) [lit.[17] bp 117–8 °C (5 mm)]; 97.8% (column A); IR, 1755, 1715 cm^{-1}; ^1H NMR δ 1.3–1.8 (m, 4 H, 2 CH_2), 1.9–2.3 (m, 6 H, 3 CH_2C=), 2.3–2.8 (m, 2 H, CH_2C=O).

7f: bp 90–92 °C (0.5 mm); 98% (column C); further purification by column chromatography (eluent, *n*-hexane), followed by bulb-to-bulb (Kugelrohr) distillation (oven temperature 105 °C (1 mm)) yielded an analytical sample, 99.5%; IR 1750, 1695 cm^{-1}; ^1H NMR δ 1.35–1.95 (m, 6 H, 3 CH_2), 2.0–2.75 (m, 8 H, 3 CH_2C=CH_2C=O); ^{13}C NMR δ 216.14, 178.22, 51.05, 42.69, 31.68, 31.50, 29.34, 28.59, 27.02, 24.23. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.29; H, 8.43. Found: C, 72.42; H, 8.38.

7g: bp 92–96 °C (0.5 mm); 97.5% (column C); analytical sample was prepared as before, 99.5%; IR 1750, 1700 cm^{-1}; ^1H NMR δ 1.3–1.85 (m, 8 H, 4 CH_2), 2.0–2.4 (m, 6 H, 3 CH_2C=), 2.4–2.7 (t, 2 H, CH_2C=O). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.33; H, 8.81. Found: C, 73.20; H, 8.81.

General Procedure for the Preparation of 8a–e: To a solution of **7** (0.05 mol) in CCl_4 (25 mL) cooled to 0 °C was added a solution of bromine (8.8 g, 0.55 mol) in CCl_4 (15 mL) over a period of 0.5 h. The resulting mixture was washed with 10% aqueous sodium thiosulfate solution and then stirred vigourously with aqueous saturated sodium bicarbonate solution (150 mL) for 6–10 h. Evaporation of the solvent followed by distillation or crystallization furnished pure **8a–e**. Alternatively, the organic layer, after washing with 10% aqueous $Na_2S_2O_3$, was evaporated, and the residue was dissolved in 1:1 THF/H_2O (25 mL) and stirred for 8–10 h at 25 °C. The mixture was then extracted with ether (100 mL), and the organic layer was dried over anhydrous Na_2SO_4 and filtered. Removal of solvent followed by distillation or crystallization provided pure **8a–e**.

8a: bp 102–4 °C (1 mm) [lit.[18] bp 102–4 °C (1.2 mm)]; 95% (column A); IR 1785, 1720 cm^{-1}; ^1H NMR δ 2.10–2.75 (m, 4 H, 2 CH_2), 2.3 (s, 3 H, CH_3), 4.82 (dd, J = 10, 2 Hz, 1 H, CHO); ^{13}C NMR δ 205.47, 175.17, 80.36, 25.59, 24.26, 22.77.

8b:[19] bp 97–100 °C (0.5 mm); 96.4% (column B); IR 1780, 1720 cm^{-1}; ^1H NMR δ 1.5 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3C=O), 2.0–2.75 (m, 4 H, 2 CH_2); ^{13}C NMR δ 206.3, 175.76, 89.08, 30.78, 28.28, 25.10, 23.30.

8c: mp 64–65 °C; 99.8% (column A); $[\alpha]^{25}_D$ +13.6° (C1, $CHCl_3$); IR 1780, 1765, and 1725 cm^{-1}; ^1H NMR δ 1.2 (s, 6 H, 2 CH_3), 1.97 (d, 1 H, J = 7.0 Hz, bridge), 2.2 (d, 1 H, J = 7.0 Hz, bridge) 2.32 (s, 3 H, CH_3C=O), 4.45 (s, 1 H, 2 CHO); ^{13}C NMR δ 205.61, 173.34, 80.34, 32.09, 29.69, 26.31, 25.05, 23.53, 14.74; GC–MS, M^+, 125 (32), 96 (95), 81 (60), 67 (46), 53 (30), 43 (100), 41 (50), 39 (37), 27 (30). Anal. Calcd for $C_9H_{12}O_3$: C, 64.29; H, 7.14. Found: C, 64.18; H, 7.10.

8d: mp 104–105 °C; 99% (column A); IR 1780, 1795 cm^{-1}; ^1H NMR δ 1.75–3.0 (m, 10 H, 5 CH_2); ^{13}C NMR δ 210.3, 177.57, 87.02, 35.24, 29.18, 28.51, 17.97; GC–MS, M^+, 154 (19), 126 (20), 98 (100), 70 (20), 56 (48), 42 (40). Anal. Calcd for $C_8H_{10}O_3$: C, 62.34; H, 6.49. Found: C, 62.20; H, 6.50.

8e: mp 49–50 °C; 99.5% (column A); IR 1780, 1725 cm^{-1}; ^1H NMR δ 1.5–2.5 (m, 8 H, 4 CH_2), 2.5–2.9 (m, 4 H, 2 CH_2); ^{13}C NMR δ 206.14, 175.78, 88.44, 38.72, 29.43, 27.93, 26.51, 21.64; GC–MS, M^+, 168 (15), 124 (35), 111 (100), 98 (40), 83 (17), 67 (15), 56 (42), 41 (27), 39 (36). Anal. Calcd for $C_9H_{12}O_3$: C, 64.29; H, 7.14. Found: C, 64.38; H, 7.06.

Preparation of 8g. To a solution of **7g** (5.4 g, 30 mmol) in CCl_4 (20 mL) was added a solution of bromine (5.28 g, 33 mmol) in CCl_4 (10 mL) at 0 °C over a period of 0.5 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with 10% aqueous $Na_2S_2O_3$ solution. The organic layer was dried as before and filtered, and the solvent was removed under aspirator vacuum to yield the acid **9b** (8.2 g, 98.7%): mp 88 °C; IR 3600–3100 (b), 1720–1710 (b) cm^{-1}; ^1H NMR δ 3.5–1.0 (m, 16 H), 7.75–7.0 (b, OH); ^{13}C NMR δ 207.96, 178.97, 72.14, 36.28, 35.62, 30.90, 30.23, 25.73, 25.50, 23.56. Anal. Calcd for $C_{11}H_{17}O_3Br$: C, 47.65; H, 6.14. Found: C, 47.45; H, 6.10.

A solution of **9b** (2.77 g, 10 mmol) in methanol (30 mL) and 0.3 M aqueous NaOH (35 mL) was refluxed for 3 h. Methanol was distilled off, and the reaction mixture was extracted with CH_2Cl_2 (2 × 30 mL). The CH_2Cl_2 layer was dried, and the solvent was removed to yield **8g** (1.66 g, 85%) as an orange liquid. This was further purified by column chromatography over silica gel, using hexane–$CHCl_3$ (9:1) as the eluent to yield **8g** as low-melting solid: IR 1780, 1710 cm^{-1}; ^1H NMR δ 1.2–2.75 (m, 16 H); ^{13}C NMR δ 212.33, 176.04, 90.22, 37.81, 35.89, 30.99, 28.44, 27.61, 26.17, 24.46, 23.01. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.35; H, 8.16. Found: C, 67.75; H, 8.27.

Preparation of 8f. To a solution of **7f** (1.66 g, 10 mmol) in CCl_4 (5 mL) was added bromine (3.2 g, 20 mmol) at 0 °C as before. Usual workup furnished the acid **11** (3.20 g, 93%): mp 99–101 °C; IR 3500–3000, 1725 cm^{-1}; ^1H NMR δ 1.85–2.82 (m, 13 H), 5.07 (dd, J = 13, 4.0 Hz, 1 H, CHBr). Anal. Calcd for $C_{10}H_{14}O_3Br_2$: C, 35.08; H, 4.09. Found: C, 35.30; H, 4.05.

A solution of **11** (0.708 g, 2 mmol) in methanol (8 mL) was refluxed with 0.3 M aqueous NaOH solution (7 mL) for 3 h. Usual workup as before yielded **10** (0.5 g, 92%): mp 107–108 °C; IR 1785, 1715 cm^{-1}; ^1H NMR δ 1.6–2.85 (m, 12 H, 6 CH_2), 4.4 (dd, J = 13.5, 5 Hz, 1 H, CHBr); ^{13}C NMR δ 204.2, 175.05, 90.47, 49.14, 37.04, 34.31, 31.58, 27.52, 27.22, 24.19. Anal. Calcd for $C_{10}H_{13}O_3Br$: C, 45.98; H, 4.98. Found: C, 45.90; H, 5.01.

To a solution of **10** (0.273 g, 1 mmol) and sodium iodide (0.375 g, 2.5 mmol) in acetonitrile (5 mL) was added freshly distilled boron trifluoride etherate (0.3 mL, 2.3 mmol) at 0 °C. The reaction mixture was stirred for 10 min at 0 °C and diluted with CH_2Cl_2 (20 mL). The organic layer was separated and dried over anhydrous Na_2SO_4. Removal of solvent provided **8f** (0.188 g, 97%): mp 71 °C; IR 1780, 1715 cm^{-1}; ^1H NMR δ 1.1–2.9 (m, 14 H); ^{13}C NMR δ 208.60, 175.69, 90.03, 39.44, 36.12, 30.65, 28.77, 27.21, 25.15, 24.14. Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.93; H, 7.69. Found: C, 65.72; H, 7.60.

Reaction of 8d,e with a Mixture of Methanesulfonic Acid–Phosphorus Pentoxide. Preparation of α-Pyrones, 17d,e. A mixture of **8d** or **8e** (5 mmol), CH_3SO_3H (2.5 mL), and phosphorous pentoxide (126 mg) was stirred at 60 °C for 2 h. The reaction mixture was cooled to 25 °C, diluted with ethyl acetate (30 mL), and washed successively with saturated aqueous $NaHCO_3$ solution (100 mL) and brine solution (20 mL). The organic layer was dried as before, and the solvent was distilled off to yield **17e** as a pale yellow solid (80% yield), which was crystallized from an ether–pentane mixture.

In the case of **17d** removal of solvent yielded a dark residue, which was extracted with petroleum ether (40–60 °C) to provide **17d** as a pale-yellow solid (50%), which was further crystallized from a ether–pentane mixture.

17d: mp 83 °C (ether–pentane); IR 1725, 1715, 1640 cm^{-1}; ^1H NMR δ 1.75–2.82 (*m*, 2 H, CH_2), 2.5–2.9 (m, 4 H, 2 CH_2C=), 6.0 (dd, J = 9, 1 Hz, 1 H, =CHC=O), 7.2 (d, J = 9 Hz, 1 H, CH=); ^{13}C NMR δ 164.91, 162.82, 142.49, 115.65, 112.42, 31.17, 29.79,

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27.96; GC-MS (70 eV), M^+, 136 (50), 108 (100), 80 (50), 79 (58), 77 (25), 66 (20), 52 (90), 39 (58), 27 (65). Anal. Calcd for $C_8H_8O_2$: C, 70.59; H, 5.88. Found: C, 70.38; H, 5.83.

17e: mp 61-2 °C (ether-pentane) (lit.[20] mp 64.5-65 °C); IR 1735, 1715, 1645 cm^{-1}; ^1H NMR δ 2.1-2.7 (m, 4 H, 2 CH_2C=), 2.55-2.05 (m, 4 H, 2 CH_2) 6.1 (d, J = 9 Hz, 1 H, =CHC=O), 7.1 (d, J = 9 Hz, 1 H, CH=C); ^{13}C NMR δ 162.7, 159.77, 146.66, 113.01, 112.54, 27.38, 25.35, 21.96, 21.57; GC-MS (70 eV), M^+, 150 (38), 122 (80), 94 (100), 79 (25), 66 (35), 52 (32), 39 (65), 27 (45), 18 (20). Anal. Calcd for $C_9H_{10}O_2$: C, 72.00; H, 6.67. Found: C, 71.83; H, 6.62.

Reaction of 8b with Polyphosphoric Acid (PPA). Preparation of the α-Pyrone, 17b. A mixture of freshly prepared PPA (27.6 g) and **8b** (1.4 g, 10 mmol) was stirred at 90 °C for 22 h. The reaction mixture was cooled to 25 °C, and ice-water (30 mL) was added. The aqueous layer was saturated with NaCl and extracted with CH_2Cl_2 (3 × 100 mL). The CH_2Cl_2 layer was washed and dried as before. Removal of solvent provided a residue (1.26 g), which was analyzed (^1H NMR) to contain **17b** (~31%) and the starting **8b** (69%). The residue was purified by column chromatography using hexane-chloroform (4:1) as eluent to yield **17b** (0.38 g, 25%), which solidified after several days in the refrigerator. Crystallization from petroleum ether (40-60 °C) yielded a white solid: mp 61-2 °C (lit.[21] mp 62-3 °C); IR, 1780, 1720, 1640 cm^{-1}; ^1H NMR δ 2.25 (s, 3 H, CH_3), 2.0 (d, J = 2 Hz, 3 H, 3 H, CH_3) 6.1 (dd, J = 11, 2 Hz, 1 H, =CHC=O), 7.18 (d, J = 11 Hz, CH=C).

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Registry No. **6a**, 3128-06-1; **6b**, 6818-07-1; **6c**, 70223-33-5; **6d**, 114942-61-9; **6e**, 118890-80-5; **6f**, 118890-81-6; **6g**, 118890-82-7; **7a**, 3740-59-8; **7b**, 4054-96-0; **7c**, 70174-49-1; **7d**, 5587-71-3; **7e**, 700-82-3; **7f**, 72925-36-1; **7g**, 63665-45-2; **8a**, 69308-41-4; **8b**, 118890-83-8; **8c**, 119006-94-9; **8d**, 118890-84-9; **8e**, 118890-85-0; **8f**, 118890-86-1; **8g**, 118890-87-2; **9b**, 118890-88-3; **10**, 118890-89-4; **11**, 118890-90-7; **17b**, 4209-44-3; **17d**, 5650-69-1; **17e**, 16326-65-1.

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Alkylation of Allylic Derivatives. 14.[1] Relationship of Double-Bond Configuration between Reactant and Product for Cross-Coupling Reactions of *Z*-Allylic Carboxylates with Organocopper Reagents

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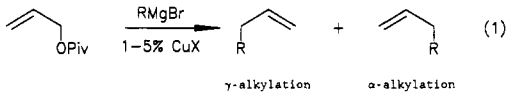
Cross-coupling reactions of alkylcuprates (sp^3 reagents) with allylic carboxylates can result in loss of double-bond configuration in the α-alkylation product. Loss of configuration occurs during the reaction, which shows that an intermediate is involved in which the double bond is temporarily relocated. With phenyl- and vinylcuprates (sp^2 reagents) the original double-bond configuration is fully preserved in all cases. This shows that the original double bond is partly retained throughout the reaction. Evidently with sp^2 reagents, oxidative addition leads directly to a π-allylcopper(III) complex (**12**).

In earlier work[1] we presented evidence that cross-coupling reactions of allylic carboxylates with organocopper reagents involve oxidative addition with allylic rearrangement to give a (γ-σ-allyl)copper(III) complex (**1**) as illustrated in Scheme I. The most important evidence in this connection is (a) γ-alkylation inevitably predominates in unbiased systems,[2] and (b) the original double-bond configuration becomes vulnerable during the reaction.[3] For example, regioselective[4] cross-coupling of *cis*-cinnamyl acetate (*cis*-**2**-OAc) with $LiCuMe_2$ gives mainly the α-alkylation product, 1-phenylpropene, with substantial loss of double-bond configuration.[3] As shown in Scheme I, α-coupling involves the temporary relocation of the double bond. Rotation of the C_β-C_γ single bond in **1** prior to allylic rearrangement to the (α-σ-allyl)copper(III) complex (**3**) results in loss of configuration.

Our original studies[3] involved the so-called stoichiometric method in which an allylic carboxylate reacts with an excess of preformed organocuprate. More recently we have found that copper(I)-catalyzed cross-coupling reactions of Grignard reagents and allylic carboxylates (eq 1)



(1)

offer important advantages over the stoichiometric method.[5] Pivalate esters are generally used in the catalytic procedures to avoid carbonyl attack by the Grignard reagent.[5]

From a comparison of stereo- and regiochemistry for the two processes, we concluded that organocuprates (e.g. $R_2CuMgBr$ for RMgBr containing 1% CuCl) are generated in the catalytic process and that the two methods are mechanistically similar.[5b]

We now have investigated the alkylation of *cis*-cinnamyl (*cis*-**2**-OPiv), *cis*-crotyl (*cis*-**4**-OPiv), and (*Z*,*E*)-3,5-heptadienyl pivalates ((*Z*,*E*)-**5**-OPiv) by the catalytic method (*n*-BuMgBr containing 1% CuCl) to determine if the or-

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