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NEW ZINC PROMOTED SYNTHETIC REACTION OF γ-BUTYROLACTONE DERIVATIVES

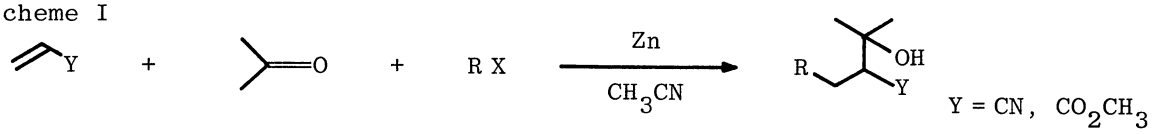
Tatsuya SHONO,* Hiroshi HAMAGUCHI, Ikuzo NISHIGUCHI, Manji SASAKI,
Tetsuya MIYAMOTO, Masatoshi MIYAMOTO, and Shumei FUJITA
Department of Synthetic Chemistry, Faculty of Engineering,
Kyoto University, Yoshida, Sakyo, Kyoto 606

Some γ-butyrolactone derivatives have been synthesized by the reaction of dimethyl maleate with carbonyl compounds in the presence of active zinc compound.

The skeleton of γ-butyrolactone is widely found as a moiety in many naturally occurring compounds and synthesis of such compounds is undoubtedly one of the most important targets in organic synthesis. Many facile methods have already been known in the synthesis of γ-butyrolactone,[1] whereas no easy method is known in the γ-alkylation of γ-butyrolactone.

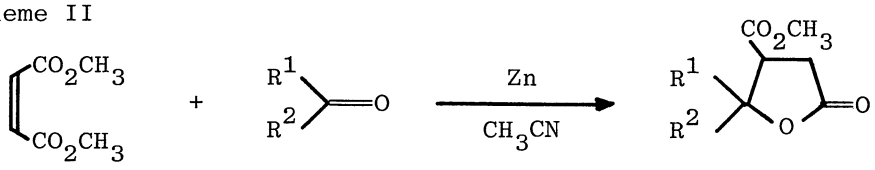
Recently, we have developed a new zinc promoted carbon-carbon bond forming reaction, in which three components, that is, α,β-unsaturated nitriles or esters, carbonyl compounds, and alkyl halides are joined in one step to give β-hydroxynitriles or esters (Scheme I).[2]

Scheme I



We wish to describe herein a new pattern of joining reaction, in which the reaction of dimethyl maleate with carbonyl compounds in the presence of active zinc compounds yields the corresponding γ-butyrolactone derivatives (Scheme II).

Scheme II

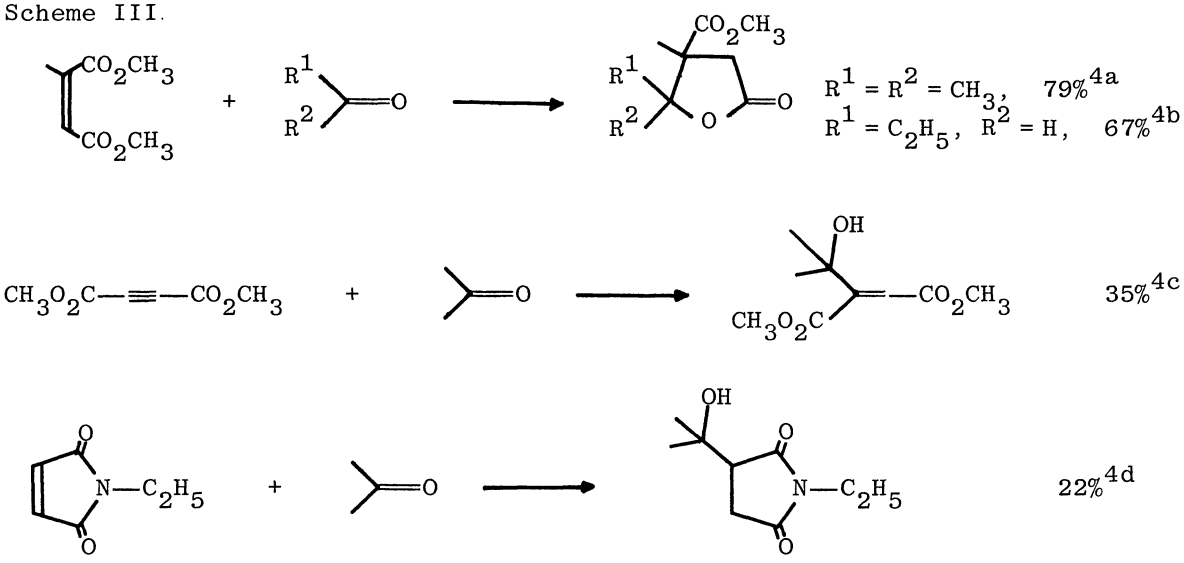


A typical procedure is as follows. Under an atmosphere of nitrogen, a mixture of 2.4 g (37 mmol) of zinc powder[3] and 2.20 ml (22 mmol) of isopropyl iodide in 20 ml of acetonitrile was refluxed with stirring for 0.5 h, and to the mixture was slowly added a solution of 1.159 g (8.04 mmol) of dimethyl maleate and 1.2 ml (16 mmol) of acetone in 5 ml of acetonitrile. After further refluxing for 3 h, the reaction mixture was poured into 20 ml of saturated aqueous solution of NH_4Cl and extracted with ether successively. The combined ethereal solution

was dried with $MgSO_4$. After evaporation of ether, treatment of the residue with column chromatography (silica gel, hexane-THF) gave β-carbomethoxy-γ,γ-dimethyl-γ-butyrolactone in a 87% yield. In a similar manner, the reaction of dimethyl maleate with a variety of ketones and aldehydes gave γ-butyrolactones in satisfactory yields (Table I).

The reaction with dimethyl fumarate also gave the same products but in rather low yields. When dimethyl citraconate was used in this reaction instead of dimethyl maleate, the coupling reaction occurred at more-substituted carbon and produced the corresponding γ-butyrolactone derivatives in moderate yields. Furthermore, this zinc promoted reductive coupling reaction was feasible for dimethyl acetylenedicarboxylate or *N*-ethylmaleimide and afforded the expected coupling products (Scheme III).

Scheme III.



Although the detailed reaction mechanism is not yet known, this zinc promoted reaction is a reductive coupling reaction and may proceed through electron transfer from some active zinc compound formed from zinc and an alkyl iodide to the carbonyl compound. Iodo compounds (*e.g.* I_2) other than isopropyl iodide can also promote this reaction but in rather low yields. In the reaction of dimethyl maleate with acetone, for instance, the use of 8 mmol of iodine instead of isopropyl iodide gave a yield of 75%. A limited number of γ-butyrolactone derivatives may be synthesized by Stobbe condensation reaction though the reaction products are generally ring-opened and dehydrated compounds.[5]

Acknowledgment

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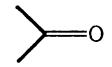
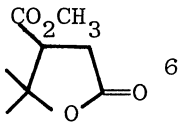
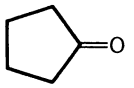
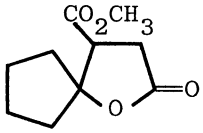
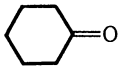
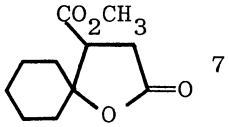
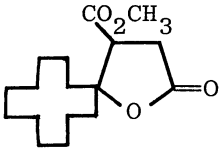
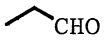
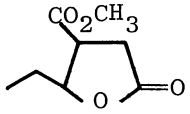
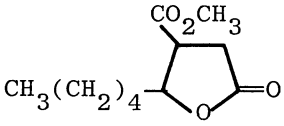
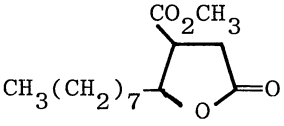
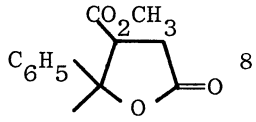
Table I. The Reaction of Dimethyl Maleate with Various Ketones or Aldehydes.

Carbonyl Compounds	Products	Yields (%)[a,b]	Bp[e] (Mp)	IR (neat) cm^{-1}
	 [6]	86	130 °C/22 mm	1780, 1730
	 [9]	74	139 °C/2 mm (38 °C)	1775, 1730
	 [7]	66	(75 °C)	1760, 1730[f]
		39	——	1770, 1730[f]
		73[c,d]	——	(a) 1775, 1730 (b) 1780, 1730
$CH_3(CH_2)_4CHO$		56[c]	——	1780, 1730
$CH_3(CH_2)_7CHO$		23[c]	——	1780, 1730
$C_6H_5COCH_3$	 [8]	70[c,d]	152 °C/4 mm	(a) 1780, 1735, 770, 700 (b) 1775, 1730, 760, 700

a. Isolated yield.
b. All the compounds gave satisfactory results in elemental analysis.
c. An equimolar mixture of two diastereomers.
d. Two stereoisomers were separated by column chromatography (Silica gel/Hexane-$AcOC_2H_5$) and gas chromatography, though the stereoconfiguration could not be assigned.
e. Kugel Rohr Distillation.
f. KBr tablet.

References

(1) For some recent examples, see:
(a) B. M. Trost, M. J. Bogdanowicz, and (in part) J. Kern, *J. Am. Chem. Soc.*, **97**, 2218 (1975).
(b) P. A. Grieco, C. -L. J. Wang, and S. D. Burke, *J. Chem. Soc., Chem. Commun.*, **1975**, 537.
(c) N. Minami and I. Kuwajima, *Tetrahedron Lett.*, **1977**, 1423.
(d) D. Caine and A. S. Frobese, *ibid.*, **1978**, 883.
(2) T. Shono, I. Nishiguchi, and M. Sasaki, *J. Am. Chem. Soc.*, **100**, 4314 (1978).
(3) Commercial 99.9% zinc powder (Institute of High Purity Chemicals, Saitama, Japan) was used without any activation.
(4) All the compounds gave satisfactory results in elemental analysis.
(a) NMR (CCl_4) δ 1.04 (s, 3H), 1.30 (s, 3H), 1.40 (s, 3H), 2.20 (d, J = 17.3 Hz, 1H), 3.15 (d, J = 17.3 Hz, 1H), 3.67 (s, 3H) ppm; IR (neat) 1770, 1730 cm^{-1}.
(b) An equimolar mixture of two diastereomers: NMR (CCl_4) δ 0.77 - 1.70 (m, 5H), 1.38 (s, 3H), 2.07 - 3.17 (m, 2H), 3.69 (s, 3H), 3.90 - 4.27 (m, 1H) ppm; IR (neat) 1770, 1730 cm^{-1}.
(c) Single isomer was obtained: NMR (CCl_4) δ 1.04 (s, 3H), 1.15 (s, 3H), 1.90 (br s, 1H, -OH), 3.61 (s, 3H), 3.68 (s, 3H), 5.57 (s, 1H) ppm; IR (neat) 3430, 1720, 1670, 1630, 870, 770 cm^{-1}.
(d) NMR (CCl_4) δ 1.02 (t, J = 6.6 Hz, 3H), 1.19 (s, 6H), 1.73 - 2.61 (m, 3H), 3.21 (br s, 1H, -OH), 3.48 (q, J = 6.6 Hz, 2H) ppm; IR (neat), 3470, 1630 cm^{-1}.
(5) W. S. Johnson and G. H. Daub in "Organic Reactions", Vol. VI, R. Adams Ed., John Wiley & Sons, Inc., New York (1951), p. 1.
(6) NMR (CCl_4) δ 1.25 (s, 3H), 1.56 (s, 3H), 2.43 - 3.33 (m, 3H), 3.71 (s, 3H) ppm.
(7) NMR (CCl_4):
(a) δ 1.03 (t, J = 7.0 Hz, 3H), 1.54 - 2.11 (m, 2H), 2.34 - 3.28 (m, 3H), 3.71 (s, 3H), 4.18 - 4.61 (q like, 1H) ppm.
(b) δ 1.04 (t, J = 6.8 Hz, 3H), 1.28 - 1.85 (m, 2H), 2.58 - 2.78 (m, 2H), 3.22 - 3.62 (m, 1H), 3.71 (s, 3H), 4.25 - 4.68 (q like, 1H) ppm.
(8) NMR (CCl_4):
(a) δ 1.56 (s, 3H), 2.87 (d of d, J = 17.4 and 9.0 Hz, 1H), 2.82 (d of d, J = 17.4 and 5.4 Hz, 1H), 3.46 (d of d, J = 9.0 and 5.4 Hz, 1H), 3.74 (s, 3H), 7.03 - 7.39 (m, 5H) ppm.
(b) δ 1.86 (br s, 3H), 2.59 - 2.86 (m, 2H), 3.16 - 3.49 (m, 1H), 3.23 (s, 3H), 7.18 (br s, 5H) ppm.
(9) The presence of a small amount of proton donor in the reaction medium was necessary in this reaction. Usually, trace of water in the solvent was sufficient to promote this reaction satisfactorily. When dry acetonitrile was used as solvent, addition of proton donor was necessary. In the reaction of dimethyl maleate in dry acetonitrile, yield was 44%, whereas addition of 8 mmol of phenol increased the yield to 73%.

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