SHORT REPORTS

J. Sci. Soc. Thailand, **1** (1975), 130–133

A CONVENIENT METHOD FOR THE SYNTHESIS OF γ-BUTYROLACTONES

V. REUTRAKUL and M. POHMAKOTR

Department of Chemistry, Faculty of Science, Mahidol University, Bangkok 4

(*Received 19 May 1975*)

Summary

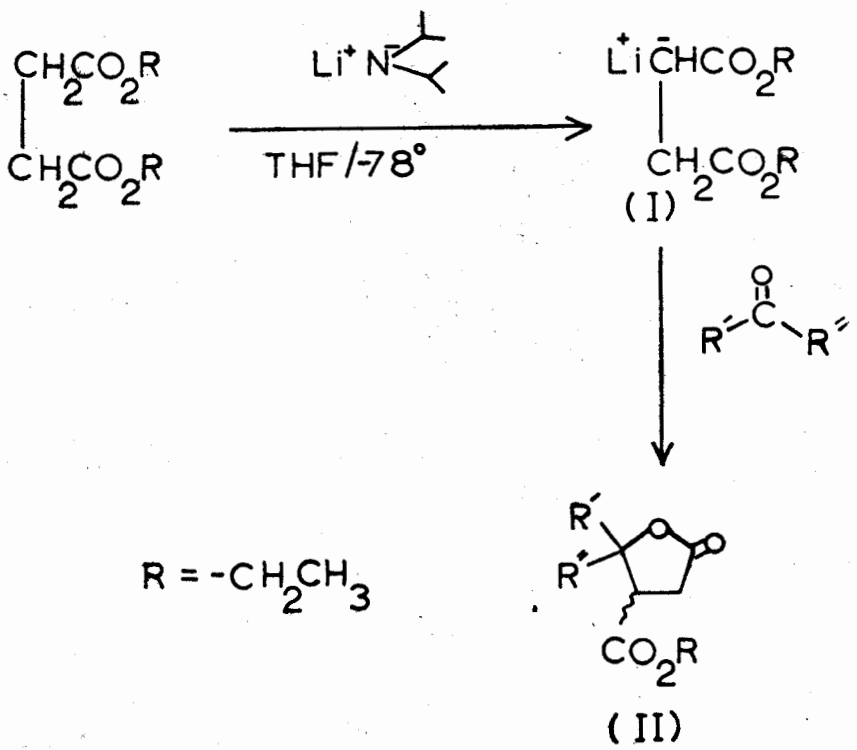
An efficient one-pot synthesis of γ -butyrolactones via *the reaction of lithio diethylsuccinate with cylic and acyclic ketones at -78° is described.*

Syntheses of γ -butyrolactones have received much attention recently owing to their importance as synthetic intermediates of natural products and other biologically active molecules[1–10]. All previously reported precedure for the synthesis of γ -butyrolactones are either multisteps or give low yields. We wish to report a simple, one-pot and high yield method for the preparation of β-carboalkoxy-γ, γ-diakyl- γ-butyrolactones.

A typical γ -butyrolactone synthesis is illustrated below for the conversion of acetone to β-carboethoxy-γ, γ-dimethyl-γ -butyrolactone. A solution of diethylsuccinate (2.5 m mole) was added at-78° to a solution of lithium diisopropylamide in tetrahydrofuran (THF) (5 mmole, 1M in THF[13]) under dry nitrogen. The reaction mixture was maintained at this temperature for 45 min, then acetone (2.5 mmole) was added. The mixture was stirred for 1.5 hr before being quenched with dilute hydrochloric acid (1.5N. 5 ml) at -78°. The aqueous solution was allowed to warm to room temperature and then the product was extracted with ether (3 x 50 ml). The combined ether extract was washed successively with water and saturated sodium chloride solution and then dried over magnesium sulfate. The ether was concentrated and the crude product was further purified by preparative thin layer chromatography on silica gel PF254 (petroleum ether/ether 3:1) to give pure β-carboethoxy-γ, γ-dimethyl-γ -butyrolactone (86%): bp 86° (2.5 mm); ir (neat), 1790, 1745 cm-1; nmr ($CDCl_3$) δ 4.2(q, 2H), 2.4–3.3(m, 3H), 1.60(s, 3H), 1 28(s, 3H), 1.32 (t, 3H).

Scheme 1 illustrates the sequence.

Scheme 1



The generation of lithio diethylsuccinate could be effected by the reaction of diethylsuccinate with either lithium diisopropylamide[11] or lithium isopropyl cyclohexylamide[12], but the former appears to be better. The yields of γ-butyrolactones from cyclic and acyclic ketones are equally good as shown in Table I.

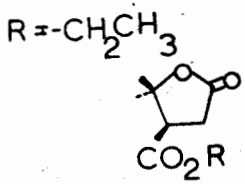
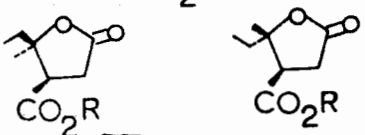
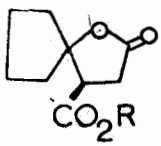
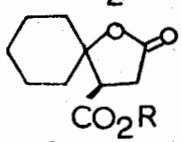
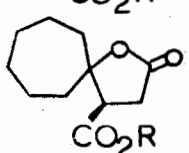
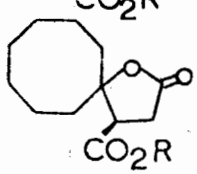
We are presently exploring in greater detail the reaction of lithio diethylsuccinate with other carbonyl compounds. The application of this method toward the synthesis of natural products[9,14,15] and prostanoid type compounds[16] are also being pursued.

Acknowledgment

We wish to thank the International Foundation for Science (IFS), Sweden, for a generous support of our program.

Table I

Conversion of carbonyl compounds into γ-butyrolactones by reaction with lithio diethylsuccinate.

Acetone			86 (bp 128°/2.5 mm)
Ethyl Methyl Ketone		(a)	83[c] (bp 130°/2 mm)
Cyclopentanone		(a)	81 (bp 128°/2 mm)
Cyclohexanone		(a)	85 (bp 146°/15 mm)
Cycloheptanone			76 (bp 160°/2 mm)
Cyclooctanone		(a)	65 (bp 174°/2 mm)

[a] These are new compounds which have been fully characterized. (V. Reutrakul and M. Pohmakotr, manuscript in preparation)

[b] Yield represents pure compound isolated by preparative thin layer chromatography on silica gel PF_{254}.

[c] The ratio of isomers is about 1:1 as indicated by NMR.

References

1. Gupta, T.K., Felix, D., Kampe, U.M. and Eschennoser A. (1972) *Helv. Chim. Acta* **55**, 2198.
2. Takeda, A., Tsuboi, S. and Ota, Y. (1973), *J. Org. Chem.* **38**, 4148.
3. Tori, S., Okamoto, T. and Takak, H. (1974) *J. Org. Chem.* **39**, 2468.

4. Meyers, A.I., Temple, D.L., Haidukewych, D. and Michelich E.D. (1974) *J. Org. Chem.* **39,** 2787.
5. Trost, B.M. (1974) *Acc. Chem. Res.* **7,** 85.
6. Sucrow, W. and Klein, U. (1975) *Chem. Ber.* **108,** 48.
7. Fukunishi, D., Inoue, Y., Kishinoto, Y. and Mashio, F. (1975) *J. Org. Chem.* **40,** 628.
8. Ellison, R.E. (1973) *Synthesis*, 397.
9. Martin, J., Watts, P.C. and Johnson, F. (1974) *J. Org. Chem.* **39,** 1676.
10. Grieco, P.A., (1975) *Synthesis*, 67.
11. Creger, P.L., (1970) *J. Amer. Chem. Soc.* **92,** 1396.
12. Rathke, R.W. and Lindert, A. (1971) *J. Amer. Chem. Soc.* **93**, 2318.
13. Cregge, R.J., Hermann, J.L., Lee. C.S., Richman, J.E. and Schlessinger, R.H. (1973) *Tetrahedron Lett.* 2425.
14. Hermann, J.L., Berger, M.H. and Schlessinger, R.H. (1973) *J. Amer. Chem. Soc.* **95,** 7923.
15. Grieco, P.A., Pogonowski, C.S., and Burke, S. (1975) *J. Org. Chem.* **40,** 542.
16. Sih, C.J., Solomon, R.G., Price, P., Sood, R. and Peruzzotti, G. (1975) *J. Amer. Chem. Soc.* **97,** 857.

บทคัดย่อ

บทความนี้บรรยายถึงวิธีสังเคราะห์ γ-butyrolactones โดยปฏิกริยา lithio diethylsuccinate กับ cyclic และ acyclic ketones.