

NEW SYNTHETIC REACTIONS: LACTONE ANNELATION

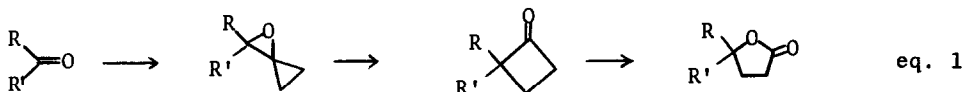
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The process of secoalkylation demonstrated the feasibility of introducing a C-C-C-N unit into  $\alpha,\beta$ -epoxy ketones.<sup>1</sup> The ability to create a synthon which reversed the electronic sense of a normal Michael acceptor promised other useful applications. We wish to report the facile conversion of aldehydes and ketones to  $\gamma$ -butyrolactones employing the equivalent of a C-C-C(=O)OH unit.



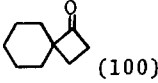
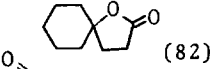
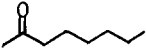
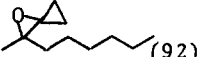
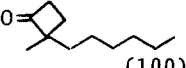
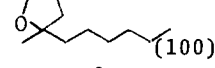
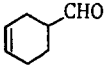

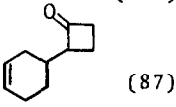
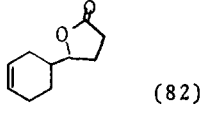


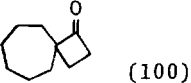
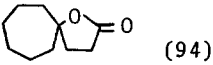
Spiroannulation of a series of carbonyl compounds (see Table I) utilizing diphenylsulfonium cyclopropylide produced the corresponding cyclobutanones after acid catalyzed rearrangement of the intermediate oxaspiropentanes.<sup>2</sup>



Cyclobutanones undergo unusually facile Baeyer-Villiger oxidations allowing the use of peroxide derivatives normally incapable of effecting such a transformation.<sup>3</sup> Thus, treatment of the cyclobutanones with basic hydrogen peroxide in methanol solution at room temperature allowed smooth conversion to the  $\gamma$ -butyrolactones in isolated yields of 82-100%. Such a rearrangement is reported utilizing hypochlorous acid.<sup>4</sup> In our hands, this reagent has led to erratic results. On the other hand, sodium hypobromite generated in situ from sodium hydroxide and bromine effected smooth rearrangement of spiro[3.6]decan-2-one to its corresponding  $\gamma$ -butyrolactone (Table I, entry 4).

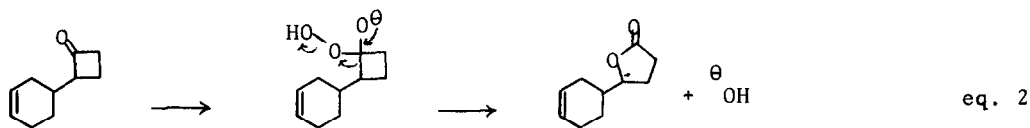
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Table I. Lactone Annelation

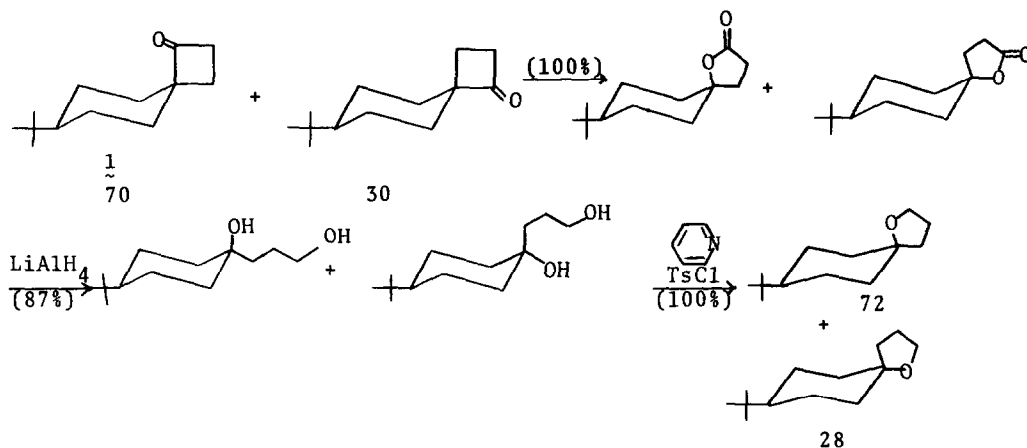
<u>Ketone</u>	<u>Oxaspiropentane</u>	<u>Cyclobutanone</u>	<u>Lactone</u>
			
			
			
			

a) Numbers in parentheses represent isolated yields.

The rearrangement appears completely analogous to the peracid catalyzed Bayer-Villager process as outlined in eq. 2.<sup>5</sup> The unusual success of hydro-



peroxide anion in effecting the rearrangement may be associated with the relief of strain energy of the four-membered ring compensating for the poor hydroxide leaving group. The data in the table indicate the same order of migratory preferences (*i.e.*, tertiary>secondary>primary) as found in the peracid reaction. Furthermore, the migration occurs with retention of configuration at the migrating carbon.<sup>6</sup> Thus, utilizing a 70:30 mixture of cyclobutanones from spiroannellation of 4-*t*-butylcyclohexanone led to a mixture of  $\gamma$ -butyrolactones which was converted as outlined into a mixture of tetrahydrofurans possessing the same composition as starting materials. Independent synthesis of the major isomer allowed the assignment of stereochemistry as shown. Since we have shown that cyclobutanone 1 is the exclusive product of spiroannellation when europium (+3) is employed to re-



arrange the precursor oxaspiropentane,<sup>7</sup> this method of lactone annelation is consequently highly stereoselective. It should be noted that use of basic hydrogen peroxide as the rearranging reagent allows the presence of double bonds (Table I, entry 3) which would interfere with normal peracid methods. The intrinsic interest in  $\gamma$ -butyrolactones as well as their important utilization as precursors to cyclopentenones<sup>8</sup> imparts special interest into this unusually facile synthetic approach.

The conversion of 2-heptanone to 4-methyl-4-n-hexyl- $\gamma$ -butyrolactone illustrates the method. As previously described, 2-heptanone was converted into 2-methyl-2-n-hexylcyclobutanone in 92% yield.<sup>1,2</sup> To a solution of 244 mg (1.45 mmol) of this cyclobutanone in 10 ml of methanol was added 443 mg (3.63 mmol) of a 30% aqueous hydrogen peroxide solution. Subsequently, 0.20 ml (1.86 mmol) of 9.28M aqueous sodium hydroxide solution was added. After 2 hr, 25 ml of a 10% aqueous hydrochloric acid solution was added. Extraction with hexane followed by evaporation *in vacuo* led to 277 mg (quantitative yield) of lactone homogeneous by vpc (11 ft x 0.25 in 8% SE-30 on Chromasorb W column) and spectral properties. Ir (CCl<sub>4</sub>) 1789 cm<sup>-1</sup>; nmr (CCl<sub>4</sub>)  $\delta$  0.90, bt, J = 2 Hz, 3H; 1.35, s, 3H; 1.2-1.6, m, 10H; 1.7-2.1, AA'BB' pattern, 2H; 2.47, AA'BB' pattern, 2H; ms m/e (%) 184(0.35), 169(4), 114(5), 100(8), 99(100), 69(7), 44(9), 43(21); calcd. for C<sub>11</sub>H<sub>20</sub>O<sub>2</sub>: 184.14632; found: 184.14639.

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#### References

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Acidic hydrogen peroxide has also been used to transform a cyclobutanone to a  $\gamma$ -butyrolactone. See P. A. Grieco, J. Org. Chem., 37, 2363 (1972).  
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