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TRANSANNULAR INTERACTIONS IN THE ACYLOIN REACTION II[1]: INTERACTION WITH KETONES

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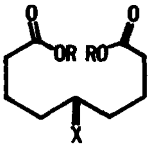
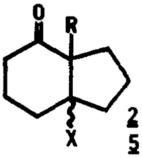
We recently reported the unexpected cyclization of methylene diester 1 under acyloin conditions to give a cis/trans mixture of bicyclic ketol 2 presumably via transannular interaction of an insipient semidione with the olefin. As part of our study on the scope of this reaction, we have studied the behavior of the analogous keto diester 4 under similar conditions and find it also undergoes transannular cyclization under certain conditions.

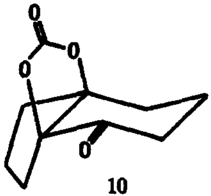
Treatment of 4 with excess sodium in refluxing toluene in the presence of the anion trapping reagent trimethylchlorosilane[2] (TMCS) resulted in isolation of fused bicyclo ketone 5 as the major product. After hydrolysis of the silyl groups, keto diol 6 was isolated by column chromatography in 27% overall yield from diester 4.



1 $X=CH_2$
4 $X=O$



2 $R=OH, X=CH_3$
5 $R=X=OSi(CH_3)_3$
6 $R=X=OH$



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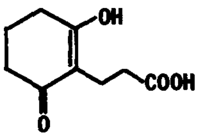
Unlike the reaction of methylene diester 1, the reaction of the keto diester 4 results in a single racemic diastereomer as determined from the cmr spectrum of diol 6. By careful comparison of the OH stretch region of the ir spectrum of 6 (3559, 3470 cm^{-1} (~.04M in CCl_4)) with that of model compounds, we were able to assign its stereochemistry as cis. Reaction of 6 with 1,1'-carbonyldiimidazole in glyme at 80° for 12 hours gave cyclic carbonate 10 (mp 87-88°; ir ($CHCl_3$) 1807 and 1729 cm^{-1}). Since the geometry of the trans isomer of diol 6 does not permit formation of a cyclic carbonate, this reaction also supports the cis assignment.

In contrast to the acyloin reaction of diester 1, no reduction was obtained when keto diester 4 was treated with sodium in refluxing toluene in the absence of TMCS. Under these conditions 35% of starting diester 4 was recovered as the only nonpolymeric material. When a catalytic amount of naphthalene was added[3] to this reaction with the intent of providing an electron carrier, however, quantitative disappearance 4 was observed. The major product obtained in this case was identified by its spectra and chemistry as 6-oxo-2-hydroxy-1-cyclohexene-1-propionic acid (7).[4]

Heating 7 resulted in its pyrolysis to give enol lactone 3 as a low melting solid (mp 52-55°). Upon treatment with hot water 3 hydrolyzed back to 7.[5]

Since it is unlikely that 7 is formed directly in the acyloin reaction, we believe that enol lactone 3 is formed as a result of a sodium naphthalide catalized condensation and that it is hydrolized under the conditions of the work-up to give acid 7.



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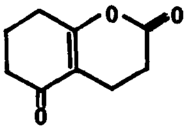

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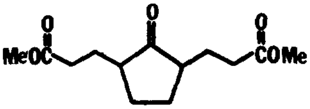

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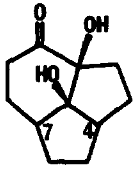

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In order to study the effects of ring strain on this acyloin cyclization, and in order to generate tricyclic materials, we treated cyclopentyl keto diester 8 with sodium in refluxing toluene in the presence of TMCS. After hydrolysis of the silyl ethers, tricyclic keto diol 9 was isolated in *ca*. 30% yield (mp 105-107°; ir (CCl_4)) 3530, 3460 and 1710 cm^{-1}; M^+ *m/e* 196).

Interestingly, although starting diester 8 was composed of a mixture of *cis* and *trans* isomers, the keto diol obtained from the reaction of 8 consisted of only one diastereomer as determined by cmr. This may have resulted from either an equilibration of starting material or products under the conditions of the reaction or, in view of the moderate yield, from the stereoselective reaction of one isomer of 8, the other giving only unidentified or intractable material. The ir spectrum of 9 indicates that the OH groups are *cis*, but the stereochemistry of the product at the 4 and 7 positions is uncertain at this time.

Further studies of the scope and mechanism of this reaction are now in progress.

References

1. For Part I, see P.Y. Johnson and M.A. Priest, J. Amer. Chem. Soc., **96**, 5618 (1974).
2. See J.J. Bloomfield, Tetrahedron Lett., 587 (1968).
3. C.D. Gutsche and I.Y.C. Tao, J. Org. Chem., **28**, 883 (1963) and C.D. Gutsche, I.Y.C. Tao, and J. Kozma, J. Org. Chem., **32**, 1782 (1967).
4. Mp 185-187° (Lit. 188°) F. Sorm, Collection Czech. Chem. Commun., **12**, 150 (1947), Chem. Abstr., **41**, 4775 (1947).
5. The synthesis by a different route, and facile hydrolysis of lactone 3 has been reported. See R.F. Gilby Jr., J. Org. Chem., **26**, 2982 (1961).