CHEMISTRY LETTERS, pp. 1473-1476, 1977. Published by the Chemical Society of Japan

# NOVEL THREE- AND ONE-CARBON RING EXPANSION REACTIONS OF A FIVE MEMBERED CARBOCYCLIC COMPOUND

Kazuo TSUZUKI, Hisanobu HASHIMOTO, Haruhisa SHIRAHAMA
and Takeshi MATSUMOTO
Department of Chemistry, Faculty of Science, Hokkaido University,
Sapporo 060

Ethyl 2-oxo-1-(2-oxopropyl)-1-cyclopentanecarboxylate, on treatment with $^t$BuOH-$^t$BuOK at rt (1h), affords unusual ring expansion products ethyl 3,5-dioxo-1-cyclooctanecarboxylate, ethyl 4-acetyl-3-oxo-1-cyclohexanecarboxylate and ethyl 2-acetyl-3-oxo-1-cyclohexanecarboxylate in 19, 40 and 12% yields, respectively.

We report here an unusual three-carbon ring expansion reaction and two, also unusual one-carbon ring expansion reactions.

In the course of synthetic studies on hirsutic acid,$^{1)}$ we treated ethyl 2-oxo-1-(2-oxopropyl)-1-cyclopentanecarboxylate$^{1)}$ **1** (1g) with $^t$BuOH-$^t$BuOK (100 cm$^3$-430mg) at rt for 1h and obtained a mixture of enolizable β-diketones, instead of the desired aldol product **2**. The mixture was separated to **A** (19%), **B** (40%) and **C** (12%), through column chromatography ($SiO_2$, ethyl acetate-benzene, 1:4) and subsequent preparative glc (QF-1). The diketones **A**,**B**,**C** were isomeric and analysed for $C_{11}H_{16}O_4$.

Compound **A** IR (neat): 1735, 1725, 1685cm$^{-1}$. NMR ($CCl_4$): δ 1.28 (3H, t, J=7Hz), 4.08 (2H, q, J=7Hz), 3.49 (2H, s), 1.50-2.30 (5H), 2.30-3.00 (4H). Intensity of the singlet peak at 3.49 was reduced by the addition of $D_2O$ containing a small amount of HCl. Similar but slow reduction of intensity was observed for the peaks around δ 2.70. Therefore, the presence of the moiety $-CH_2COCH_2COCH_2-$ was shown and accordingly the structure **3** was suggested for compound A.

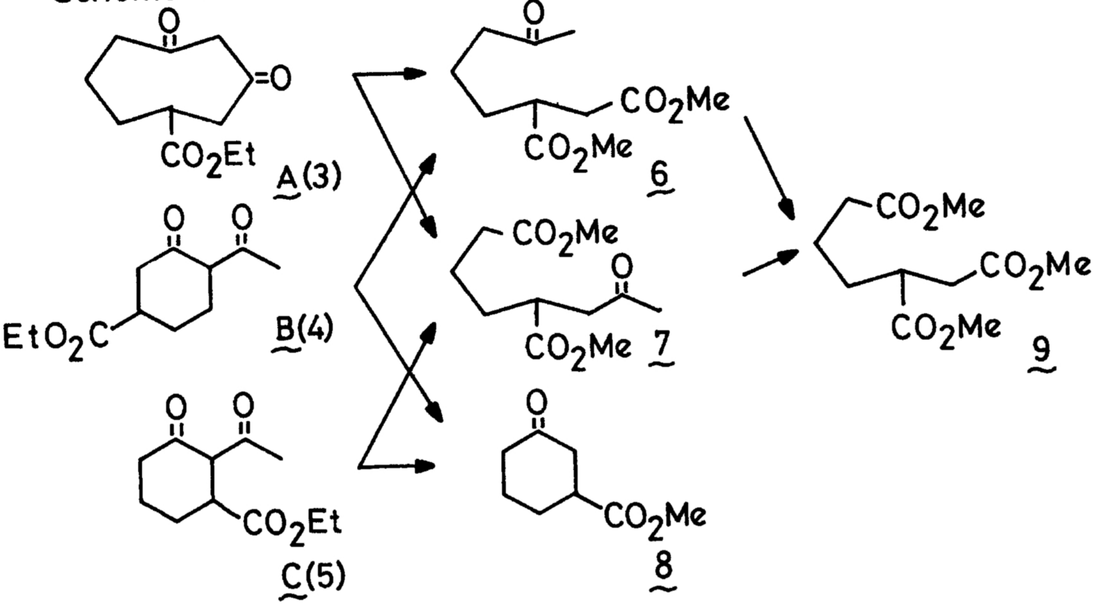
Compound **B** IR (neat): 1735, 1610cm$^{-1}$. NMR ($CCl_4$): δ 1.28 (3H, t, J=7Hz), 4.11 (2H, q, J=7Hz), 2.07 (3H, s), 15.73 (1H, s), 1.60-2.20 (2H), 2.20-2.80 (5H).

**Compound C** IR (neat): 1735, 1610cm$^{-1}$. NMR ($CCl_4$): $\delta$ 1.28 (3H, t, J=7Hz), 4.10 (2H, q, J=7Hz), 1.99 (3H, s), 3.40 (1H, dd, J=5 and 3Hz), 16.7 (1H, s), 1.50-2.10 (4H), 2.10-2.60 (2H). These spectral data show that the both compounds are strongly enolized methyl ketones containing a ethoxycarbonyl group, such as 4 and 5.

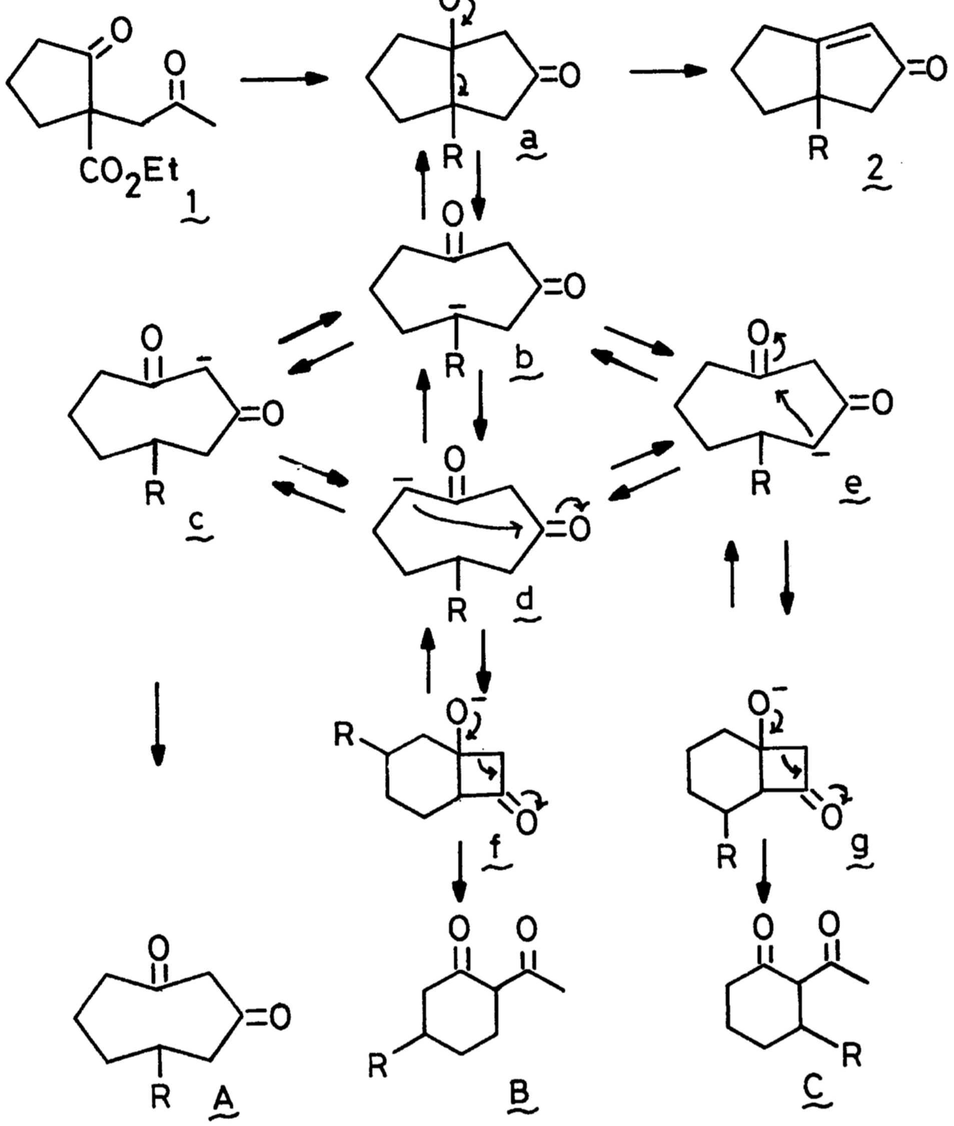
That the structures of A, B and C are actually expressed respectively by 3, 4 and 5 was demonstrated by the following transformations (Scheme 1). Each of compounds A, B and C was treated with 10% aq. KOH solution (rt, 20h) and the products were esterified with $CH_2N_2$. Compound A gave a mixture of isomeric diesters 6[2,4] and 7[4,5] (65 and 15% yields, respectively). Compound B afforded a mixture of 3-methoxycarbonylcyclohexanone 8[3] (25%) and the diester 6 (55%), while compound C gave 7 (85%) and 8 ( 1%, detected by glc). Oxidation of diesters 6 and 7 by the iodoform reaction, followed by esterification with $CH_2N_2$, furnished the same triester 9.[4,6] The esters 6 and 7 were identified respectively with authentic samples prepared by unambiguous procedures.[7]

A possible explanation for the formation of compound A, B and C is shown in Scheme 2. Cyclooctyl anions c (or b), d and e, produced by C·3a-C·6a bond fission of intermediary aldol[8] a and subsequent proton transfer, would give rise to A, B and C, respectively, directly (in the case of A) or through cyclobutanol intermediates[9] f and g (in the case of B and C). Compound A is not the intermediate for B and C. Treatment of A with $^t$BuOK under the above described conditions did not afford compounds B and C, and A was recovered unchanged, probably because of preferential formation of the stable anion c, rather than b, d and e. However, at reflux (0.5 h) under the otherwise same conditions, A gave B (10%) and C (5%), together with the conjugated ketone 2 (20%), supporting the assumed equilibria among a, b and c. It seems interesting that in contrast to the reaction by means of $^t$BuOK at rt, the reaction with NaH-benzene (rt or 80°) affords the cojugated enone as a main product (50%).[1] The reason for this remarkable solvent-base dependence is however not clear at present.

Scheme 1



Scheme 2



R = $CO_2Et$

## References and Notes

1) H. Hashimoto, K. Tsuzuki, F. Sakan, H. Shirahama, and T. Matsumoto, Tetrahedron Lett., **1974**, 3745.

2) δ ($CCl_4$) 2.07 (3H, s), 3.57 (3H, s), 3.59 (3H, s); ν (neat) 1740, 1725$cm^{-1}$.

3) D. Banerjee, J. Dutta, and G. Bagavant, Proc. Indian Acad. Sci., **46A**, 80 (1957).

4) Satisfactory analytical data were obtained for this compound.

5) δ ($CCl_4$) 2.03 (3H, s), 3.59 (3H, s), 3.62 (3H, s); ν (neat) 1740, 1725$cm^{-1}$.

6) δ ($CCl_4$) 3.57 (3H, s), 3.59 (3H, s), 3.62 (3H, s); ν (neat) 1740$cm^{-1}$.

7) Mehtyl ester **6** was prepared from **1** through treatment with KOH and subsequent esterification with $CH_2N_2$. The corresponding ethyl ester has been obtained in a different manner: R. Glein and M. Chignac, Bull. Soc. Chim. Fr., **1965**, 139. Compound **7** was obtained through the sequence: 2-cyclohexenone → 3-cyanocyclohexanone (KCN) → **7** (KOH, $CH_2N_2$).

8) Another example of the 3a,6a bond fission in a suitably functionalized 3a,6a disubstituted octahydropentalene derivative is described in the accompanying paper. In the case of ethyl 2-oxo-1-(2-oxopropyl)-1-cyclohexanecarboxylate ($^t$BuOH-$^t$BuOK), analogous bond fission was not observed and the expected product of the type **2** was obtained; W. G. Dauben, J. W. McFarland, and J. B. Rogan, J. Org. Chem., **26**, 297 (1961).

9) Acid catalysed interconversion of the cyclooctane-, bicyclo[3.3.0]octane- and bicyclo[4.2.0]octane-skeletons has been reported: Y. Ohfune, H. Shirahama, and T. Matsumoto, Tetrahedron Lett., **1976**, 2795.

(Received October 12, 1977)