

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

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Ethyl 2-oxo-1-(2-oxopropyl)-1-cyclopentanecarboxylate, on treatment with $t\text{BuOH}-t\text{BuOK}$ 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-cyclopentanecarboxylate¹⁾ 1 (1g) with $t\text{BuOH}-t\text{BuOK}$ (100 cm³-430mg) 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 $\text{C}_{11}\text{H}_{16}\text{O}_4$.

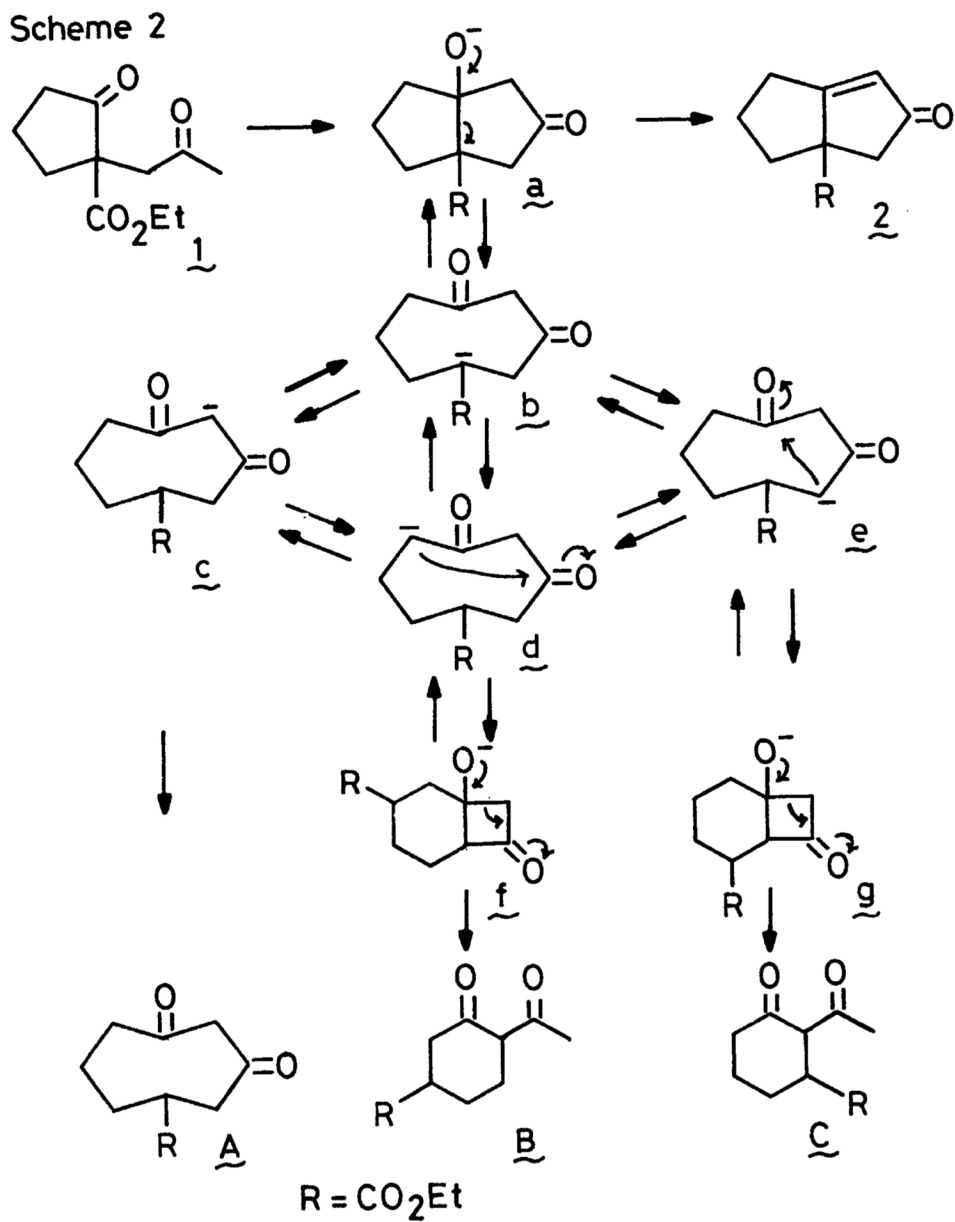
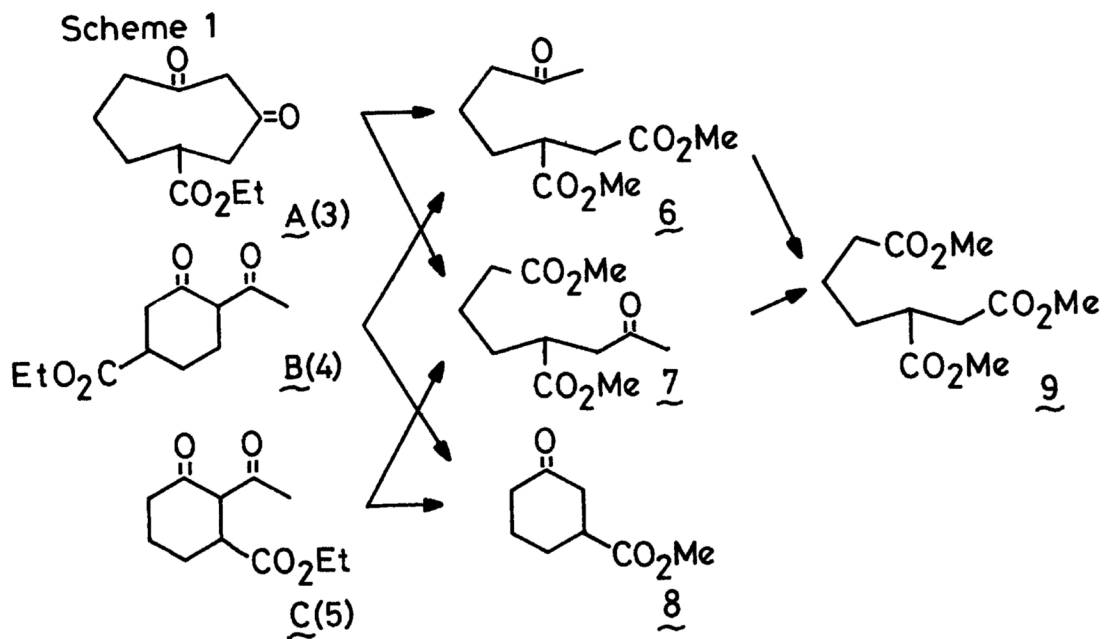
Compound A IR (neat): 1735, 1725, 1685cm⁻¹. NMR (CCl_4): δ 1.28 (3H, t, $J=7\text{Hz}$), 4.08 (2H, q, $J=7\text{Hz}$), 3.49 (2H, s), 1.50-2.30 (5H), 2.30-3.00 (4H). Intensity of the singlet peak at 3.49 was reduced by the addition of D_2O containing a small amount of HCl. Similar but slow reduction of intensity was observed for the peaks around δ 2.70. Therefore, the presence of the moiety $-\text{CH}_2\text{COCH}_2\text{COCH}_2-$ 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, $J=7\text{Hz}$), 4.11 (2H, q, $J=7\text{Hz}$), 2.07 (3H, s), 15.73 (1H, s), 1.60-2.20 (2H), 2.20-2.80 (5H).

Compound C IR (neat): 1735, 1610 cm^{-1} . NMR (CCl_4): δ 1.28 (3H, t, $J=7\text{Hz}$), 4.10 (2H, q, $J=7\text{Hz}$), 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 8³⁾ (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 aldol⁸⁾ a and subsequent proton transfer, would give rise to A, B and C, respectively, directly (in the case of A) or through cyclobutanol intermediates⁹⁾ f and g (in the case of B and C). Compound A is not the intermediate for B and C. Treatment of A with $t\text{BuOK}$ 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 $t\text{BuOK}$ at rt, the reaction with NaH-benzene (rt or 80°) affords the conjugated enone as a main product (50%).¹⁾ The reason for this remarkable solvent-base dependence is however not clear at present.



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) Methyl 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 $\rightarrow$ 3-cyanocyclohexanone (KCN) $\rightarrow$ 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 ($^t\text{BuOH}$ - $^t\text{BuOK}$), 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. Ohfuné, H. Shirahama, and T. Matsumoto, *Tetrahedron Lett.*, 1976, 2795.

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