135. Studies on the Synthetic Usefulness of the Nitro Function

Part I

A Novel Cyclopentenone Ring Annelation

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(20.II.84)

Summary

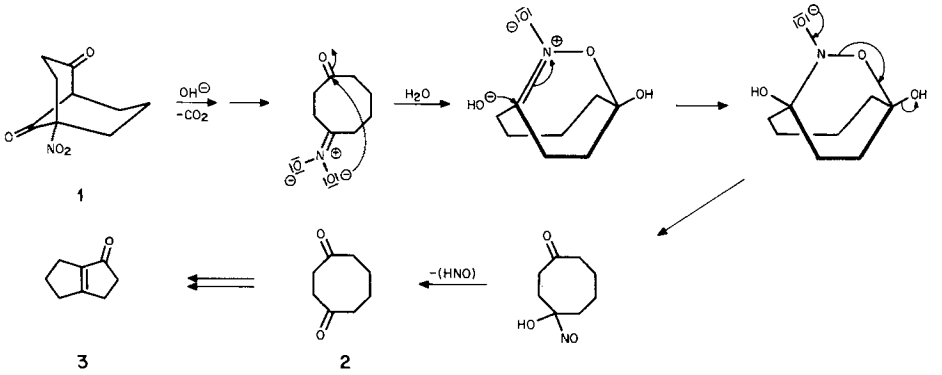
A novel cyclopentenone ring annelation reaction is described. The treatment of the nitro compound **13** with aqueous sodium hydroxide in the presence of a phase-transfer catalyst furnished **14a** in one step. Similar treatment of **7** led to **8**, the reaction of which with *t*-BuOK afforded **9a** without purification in high yield.

The usefulness of the nitro group in organic syntheses has been demonstrated by many authors [1]. For the conversion of the nitro to the oxo group under alkaline reaction conditions, only a few examples are known [2], although several methods using various conditions have been mentioned in the literature [3]. In [4], we reported the conversion of 5-nitrobicyclo[3.3.1]nonan-2,9-dione (**1**) to bicyclo[3.3.0]oct-1(5)en-2-one (**3**) under mild alkaline conditions ($K_2CO_3/H_2O/70°$). The reaction very probably proceeds *via* 1,4-octadione (**2**) which undergoes an aldol condensation. A proposed reaction mechanism, based on the neighbourhood of the aci-nitro and oxo group in the 8-membered ring, is outlined in *Scheme 1*. Attempting to generalize these reaction conditions applied in a specific case, we studied the reaction sequence presented in *Scheme 2*.

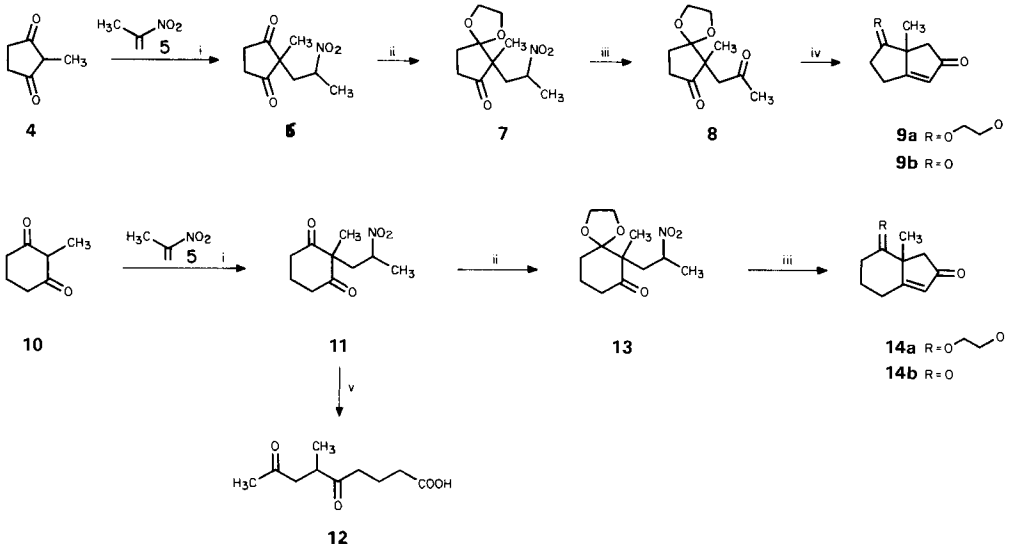
Condensation of 2-methyl-1,3-cyclopentanedione (**4**) with 2-nitropropene (**5**) in the presence of catalytic amounts of $(C_4H_9)_3P$ (acetonitrile, 20°, 10 h, Ar) gave the *Michael* adduct **6**[1]) in quantitative yield [5]. Under the same reaction conditions, 2-methyl-1,3-cyclohexanedione (**10**) was converted to **11**[1]). Attempts were made to transform **6** and **11** under mild alkaline reaction conditions to the ring annelation products **9b** and **14b**, respectively. In both cases, the treatment of these adducts with 25% aq. K_2CO_3-solution at 75–80° [4] was not successful: compound **6** gave no detectable products, and **11**

[1]) *Data of* **6**: IR ($CHCl_3$): 1725, 1540. ^{1}H-NMR (60 MHz, $CDCl_3$): 4.9–4.2 (*m*, 1H); 1.5 (*d*, 3H); 1.2 (*s*, 3H). MS (70 eV): 199 (M^+). *Data of* **11**: IR ($CHCl_3$): 1731, 1696, 1550. ^{1}H-NMR (60 MHz, $CDCl_3$): 4.9–4.2 (*m*, 1H); 1.5 (*d*, 3H); 1.3 (*s*, 3H). MS (70 eV): 213 (0, M^+), 167 ($[M-46]^+$).

Scheme 1

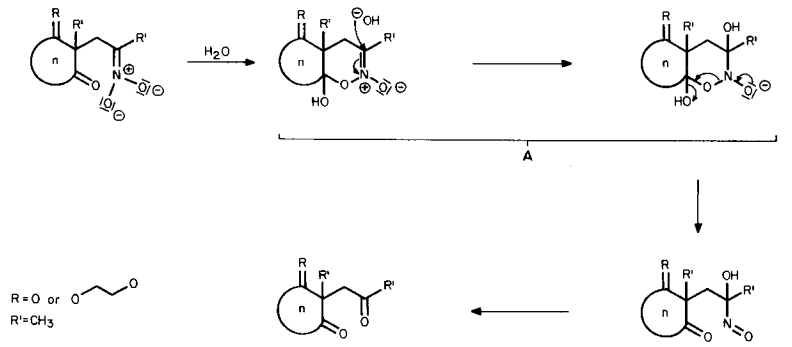


Scheme 2



i: Bu_3P; ii: $HOCH_2CH_2OH$, TsOH; iii: 50% NaOH, Bu_4NBr; iv: *t*-BuOK/*t*-BuOH; v: 25% K_2CO_3/H_2O

Scheme 3



afforded 6-methyl-5,8-dioxononanoic acid (**12**)[2]) in quantitative yield[3]). After monoacetalization of **6**, the nitro group in **7**[4]) could be converted to an oxo group using 50% aq. NaOH containing small amounts of Bu_4NBr (0.04 mol). The resulting diketone **8**[5]) was treated without purification with *t*-BuOK/*t*-BuOH (20°, 3 h) to give the condensation product **9a**[6]) [8] in 73% overall yield. Application of the same phase-transfer procedures to the 6-membered **13**[7]), prepared from **11**, led directly to **14a**[7]) [8] (93% yield) without detection of the corresponding diketone.

A reaction mechanism of the transformation of **7** to **8** and for the 6-membered analog is proposed in *Scheme 3*[8]). We suppose that the nitro group reacts in the aci-nitro form, and, under the influence of the neighbouring oxo group, the cyclic intermediate **A** is formed[9]). Intermediate **A** decomposes to the diketone.

We believe that this new method will facilitate the synthesis of natural products containing cyclopentenone moieties [10].

A part of this work was supported by the *Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung* which is thankfully acknowledged. *Y.N.* is indebted to Prof. *Y. Morita* and Dr. *H. Ito* of Josai University for helpful discussions and especially to Prof. *Y. Morita* for his encouragement throughout this work.

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[2]) *Data of* **12**: IR ($CHCl_3$): 3500, 1780–1680 br. ^{1}H-NMR (60 MHz, $CDCl_3$): 10.1 (br. *s*, 1H); 2.2 (*s*, 3H); 1.1 (*d*, 3H). MS (70 eV): 202 (M^+).

[3]) The behaviour of 2,2-disubstituted 1,3-cyclohexanedione derivatives under alkaline reaction conditions was studied earlier [6]. Formation of compounds of type **12** from analogs of **11** in the presence of acid is well-known [7].

[4]) *Data of* **7**: IR ($CHCl_3$): 1742, 1545. ^{1}H-NMR (60 MHz, $CDCl_3$): 3.9 (*s*, 4H); 1.5 (*d*, 3H); 1.1 (*s*, 3H).

[5]) *Data of* **8**: IR ($CHCl_3$): 1740, 1710. ^{1}H-NMR (60 MHz, $CDCl_3$): 2.11 (*s*, 3H).

[6]) *Data of* **9a**: IR ($CHCl_3$): 1705, 1630. ^{1}H-NMR (60 MHz, $CDCl_3$): 5.8 (narrow *m*, 1H); 3.9 (*s*, 4H); 1.3 (*s*, 3H). MS (70 eV): 194 (M^+).

[7]) *Data of* **13**: IR ($CHCl_3$): 1717, 1550. ^{1}H-NMR (60 MHz, $CDCl_3$): 4.0 (*s*, 4H); 1.5 (*d*, 3H); 1.1 (*s*, 3H). *Data of* **14a**: IR ($CHCl_3$): 1705, 1630. ^{1}H-NMR (60 MHz, $CDCl_3$): 5.7 (narrow *m*, 1H); 3.9 (*s*, 4H); 1.4 (*s*, 3H). MS (70 eV): 208 (M^+).

[8]) Similar results and an alternative reaction mechanism in aprotic solvents under alkaline conditions have been reported by *Yoshikoshi et al.* [2d] [9].

[9]) It was reported that the *Nef* reaction performed under alkaline conditions, explained by a neighbouring group participation, depends on the basicity and concentration of alkaline [2c]; these phenomena were also observed in our experiments.

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