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ACID-CATALYZED CYCLIZATION OF CROSS-CONJUGATED DIENONE MOIETY TO CYCLOPENTENONES

Shigeo HIRANO, Tamejiro HIYAMA, and Hitosi NOZAKI
Department of Industrial Chemistry, Kyoto University, Kyoto, Yoshida, Japan.

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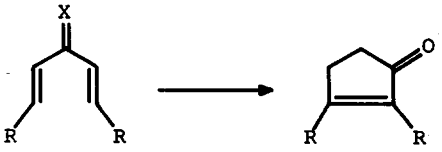
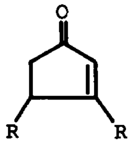
Conjugated cyclopentenones (III) substituted at 2- and 3-positions involve such important compounds as jasmone and prostaglandin B family,[1] and also intermediates for synthesizing muscone[2] or [n]metacyclophanes.[3] This communication discloses a new route to III from cross-conjugated, symmetrical dienones (I) or their ethylene acetals (II).



I (X = O), II (X = OCH_2CH_2O) III

a: R = Et
b: R = $-(CH_2)_7-$
c: R = $-(CH_2)_5-$

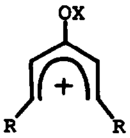


IV

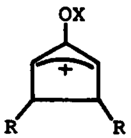
According to the procedure A, a dienone (I), or preferably, the acetal (II) was treated with H_3PO_4-HCOOH (1:1, 90°, 2-3 hr). After usual work-up 2,3-dialkyl-2-cyclopentenone (III) was obtained as the sole product or at least as the major product. When I or II was exposed to less nucleophilic acid (HBr-AcOH, 1:3, 80-90°, 2-3 hr) (procedure B), the amount of the by-product IV increased considerably. The results are as follows: [starting material, procedure, product (Yield[4a])]: [Ia,[4c] A, IIIa[4c,d] (77%)]; [IIa,[4c] A, IIIa (67%)]; [IIb,[4c] A, IIIb[4e] (67%, 63%[4b])]; [IIc,[4c] A, IIIc[4c,f] (58%) and IVc[4i] (6%)]; [Ia, B, IIIa (55%, 41%[4b]) and IVa[4g] (15%, 11%[4b])]; [Ib,[4c] B, IIIb (41%[4b]) and IVb[4h] (5%[4b])]; [IIa, B, IIIa (43%) and IVa (9%)]; [IIb, B, IIIb (55%) and IVb (6%)]; [IIc, B, IIIc (47%) and IVc (37%)].

Although the formation of the by-product IV could be ascribed to the Nazarov-type cyclization[5] of hydroxypentadienyl cation (V)[6], followed by the deprotonation of the resulting hydroxyallyl cation VI, this mechanism would not explain the production of III requiring the "shift" of a carbonyl group.[7] The present conversion is rationalized by assuming the attack of the hydroxylic solvent (water, carboxylic acid, or phosphoric acid) on the hydroxyallyl cation VI to yield VII, which is then converted to acyloin VIII[8] and to IX. Dehydration and isomerization of IX afford III.[9]

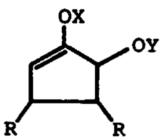
A typical procedure for a large scale synthesis is exemplified by the preparation of IIIb. Cyclododeca-2,11-dienone ethylene acetal (IIb)[10] (22.2 g, 0.1 mol) was dissolved in 85% phosphoric acid (100 ml) and 90% formic acid (100 ml), and the mixture heated at 90° for 3 hr under N_2 atm. The reaction mixture



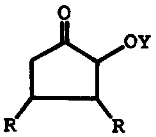
V



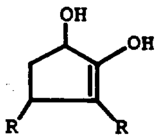
VI



VII



VIII



IX

X = H or CH_2CH_2OH, Y = H, COMe, COH, or $PO(OH)_2$

was then treated with water (200 ml) and heated again at 90° for an additional 1 hr. Extraction with ether (50 ml x 3 times), followed by distillation, gave bicyclic cyclopentenone IIIb (11.2 g, 63% yield, bp 125°/5 mm) which proved to be pure on glc assay and gave identical spectra as the authentic specimen.[3a]

References and Footnotes

1. R. A. Ellison, *Synthesis*, 397 (1973).
2. A. Eschenmoser, D. Felix, and G. Ohloff, *Helv. Chim. Acta*, **50**, 708 (1967); D. Felix, J. Schreiber, G. Ohloff, and A. Eschenmoser, *ibid.*, **54**, 2896 (1971).
3. (a) S. Fujita, S. Hirano, and H. Nozaki, *Tetrahedron Lett.*, 403 (1972). (b) S. Hirano, T. Hiyama, S. Fujita, and H. Nozaki, *Chemistry Lett.*, 707 (1972).
4. (a) Estimated by glc unless specified. (b) Isolation yield. (c) The new compound was identified analytically and/or spectrometrically. (d) Ir (neat): 1698, 1644 cm^{-1}. (e) Ir (neat): 1696, 1646 cm^{-1}. (f) Ir (neat): 1695, 1646 cm^{-1}. (g) Ir ($CHCl_3$): 1685, 1613 cm^{-1}. (h) Ir ($CHCl_3$): 1682, 1610 cm^{-1}. (i) Ir ($CHCl_3$): 1680, 1603 cm^{-1}.
5. (a) I. N. Nazarov, I. I. Zaretskaya, and T. I. Sorkina, *Zh. Obshch. Khim.*, **30**, 746 (1960); *Chem. Abstr.*, **55**, 524h (1961). (b) E. A. Braude and J. A. Coles, *J. Chem. Soc.*, 1430 (1952). (c) C. W. Shoppee and B. J. A. Cooke, *ibid. Perkin I*, 2271 (1972).
6. R. B. Woodward and R. Hoffmann, "*The Conservation of Orbital Symmetry*", Academic Press, New York, N.Y., 1970, p 58.
7. Thus we can predict that the acid-catalyzed cyclization of 2,5-heptadien-4-one should yield 2,3-dimethyl-2-cyclopentenone instead of the recorded isomer, 3,4-dimethyl-2-cyclopentenone (N. Jones and H. T. Taylor, *J. Chem. Soc.*, 1345 (1961)). Actually, a question on the previously assigned structure has been raised (J. M. Conia and M. L. Leriverend, *Bull. Soc. Chim. Fr.*, 2981 (1970)).
8. The products in the procedure B were often contaminated by a trace of acetoxycyclopentanone probably due to insufficient hydrolysis of the intermediate VIII.
9. The mechanism is possibly supported by the fact that 2-hydroxy-3-methylcyclopentanone readily dehydrated regioselectively to yield 2-methyl-2-cyclopentenone under acidic condition or by simple distillation. The general synthetic application of this simple dehydration reaction to 2,3-unsymmetrically disubstituted 2-cyclopentenones is being explored.
10. The dienone acetal IIb was prepared from cyclododecanone ethylene acetal by means of dibromination and subsequent dehydrobromination in 95% overall yield.