

NOVEL REARRANGEMENT OF TWISTED 2,4-DI-ALKYL 2-TRANS-4-TRANS PENTADIENALS: AN APPROACH TO
CYCLOPENTENONES BASED ON MOLECULAR MECHANICAL CONSIDERATION

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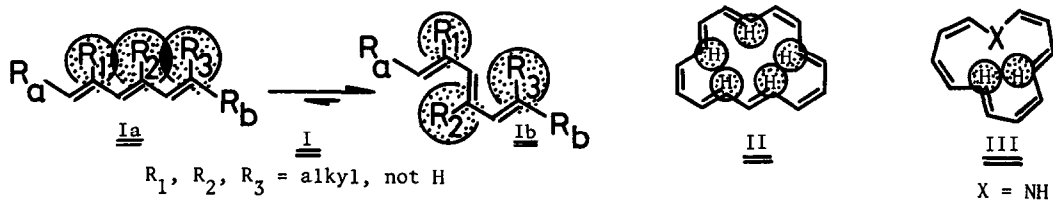
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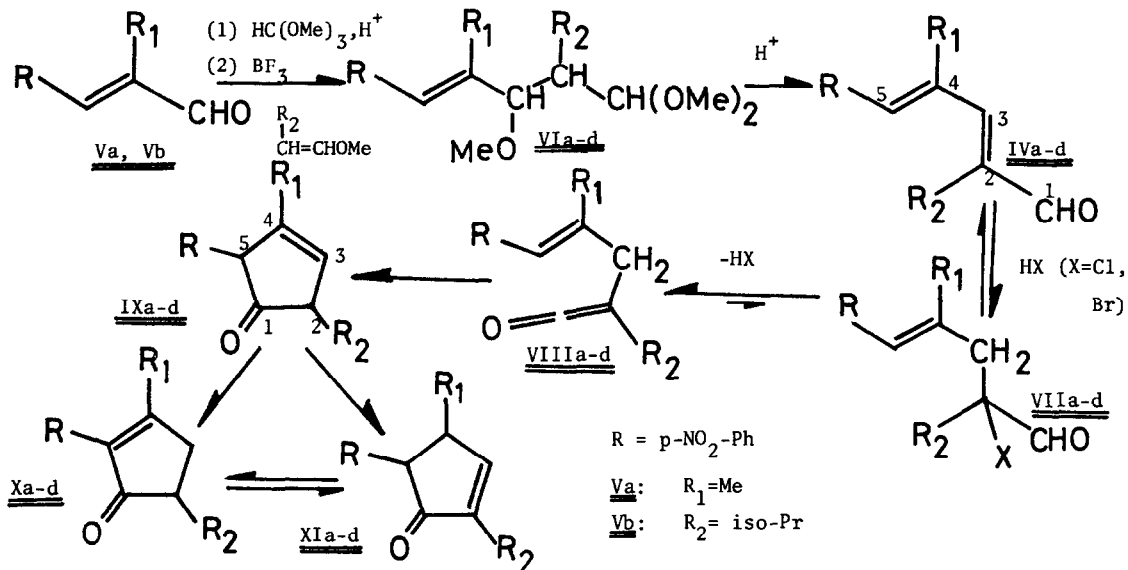
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Summary: Rearrangement of 2,4-di-trans-pentadienals IVa-d was described as a consequence of the successive alkyl substitutions on the C-2 and C-4 positions. ¹H-FT nmr spectroscopy suggested that the reaction involves ketene VIII as an intermediate.

Hydrogen-hydrogen repulsive interactions occurred in annulenes (for example, II and III^{1a}) not only specify the thermodynamic stabilities of the molecules, but they are also vital for the determination of the dynamic equilibrium among possible geometrical isomers^{1b}). Similar circumstances may arise, when bulky groups are introduced on linear conjugated system I. Molecular mechanical considerations suggest that Ib becomes favoured than Ia, and cyclization of Ib may be induced, if a suitable reaction path is opened for the transformation. As model reaction, we report novel rearrangement of 5-(p-nitrophenyl)-2,4-di-alkyl-pentadienals IVa-d to the corresponding cyclic enones IXa-d and their tautomers Xa-d and XIa-d (see Scheme 1).



2,4-Di-alkyl-pentadienals IVa-d were prepared by the homologation of the corresponding 2-alkyl-cinnamaldehydes Va-b according to the alkyl enolether method. The 2-trans-4-trans configuration of IVa-d rests on the observed chemical shifts of the trans aldehydic protons appeared at δ 9.90 - 9.80. No formation of the corresponding 2-cis isomers was observed, in which the aldehyde protons should be resonated at lower field (expected value: 10.2 - 10.5³). Dienals IVa-d are highly restricted to possess 3,4-s-cis configuration to relieve the unfavourable H-H



Scheme 1. IV, VI, VII, VIII, IX, X and XI: a: $R_1 = R_2 = \text{Me}$; b: $R_1 = \text{Me}$, $R_2 = \text{iso-Pr}$; c: $R_1 = \text{iso-Pr}$, $R_2 = \text{Me}$; d: $R_1 = R_2 = \text{iso-Pr}$.

interactions, since the 3,4-*s-cis*-configuration of a similar side chain was reported to be ca. 6 kcal/mole more stable than the 3,4-*s-trans* isomer⁴). In agreement with the inspections of the CPK models, electronic spectra indicated that IVa-d suffer from considerable twists from planarity. Hypsochromic shifts observed were increased in the following order; 4nm in IVb, 14nm in IVc, and 37nm in IVd, as compared with the absorption maximum of IVa (λ_{max} 326nm in EtOH).

Rearrangement of IVa-d could be realized most simply by the addition of few drops of conc. HX (X = Cl or Br) in THF at 40°. Following features were collected.

- (1) The introduction of two alkyl groups on the 2 and 4 positions of IVa-d is indispensable.
- (2) The addition of HX does not catalyze the isomerization of IVa-d to give the 2-*cis*-4-*trans* isomers. This means that the rearrangement does not be preceded by the isomerisation.
- (3) The use of CF_3COOH or *p*-TsOH in place of HX does not lead to the effective cyclization, even enforced conditions were employed [for example, 90° for 4 hrs].
- (4) The rearrangement occurs also in such weak acidic medium as was used in the hydrolysis of ethereal acetal VIa with a diminished rate[†] [NaOAc (10 g) in 70% aq. AcOH (100 ml), 90°]
- (5) Compounds IXa-d were obtained as primary products, if temperature was controlled below 45° (in DMSO- d_6). On heating to 60°, they were converted to the mixtures consisted of Xa-d and XIa-d in a ratio of ca. 1:1, respectively.

The cyclization of IVa was studied by the time course ¹H-FT nmr spectroscopy at 45°. This experiment enables us to convince that the rearrangement involves a ketene intermediate VIIIa.

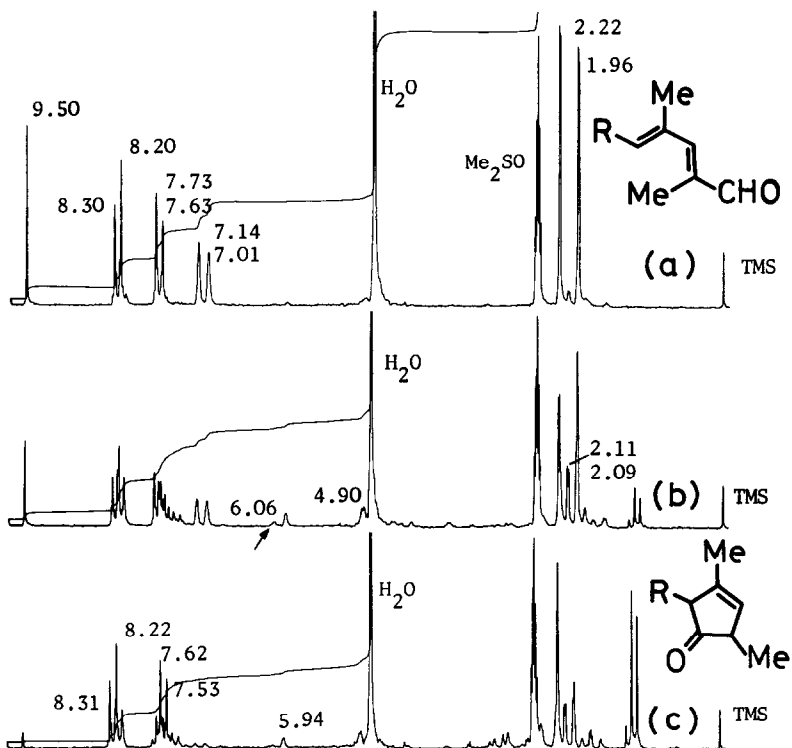


Fig. 1 ¹H FT nmr time course spectra of the cyclization of IVa in DMSO-d₆ at 45°; (a) after 50 sec from the addition of HCl (b) after 16 min. (c) after 66 min.

As shown in Fig. 1b, VIIIa exists in a steady state concentration through the cyclization step, exhibiting two proton singlet at δ 4.90 for CH₂ protons, one proton singlet at δ 6.06 for the olefinic proton, both of them are broadened by allyl couplings, and two singlets assignable to the methyl protons attached on the sp² bonds at δ 2.11 and 2.09, respectively. The rate of the cyclization was found to be proportional to the concentration of HCl added. We propose, on the basis of the intermediacy of ketene VIII, the mechanism of this reaction. In the first place, the addition of HX occurs on the C-2 and C-3 positions of dienal IVa to form VIIa. Once the HX-adduct is formed, it successively undergoes HX-elimination in a competitive reaction to give dienal IVa (via backward elimination) and ketene VIIIa (via HX elimination from aldehyde H of VIIa), thermodynamically controlled product. This addition-elimination mechanism was also supported by the experimental result that the doublet of the C-2 methyl protons of IXa ($J = 9$ Hz) changed into a singlet at δ 1.15, when DCl was used for the cyclization.

Our model reaction can be concluded as follow: (a) the key leading to the cyclization is attributable to (i) the nonplanar twisted conformation of IV, and (ii) the strain relief of the HX-adduct VII. This makes a marked contrast with the previously reported ketene form-

ations from pentadienals⁵⁾ and pentaynenals⁶⁾ were only documented in pyrolysis conditions (400-700°C); (b) the subsequent electrocyclic reactions, entropically favoured processes to give the kinetic isomers IXa-d, proceed in excellent yield under extremely mild conditions. Proximity and orientation effects may facilitate this rearrangement⁷⁾; (c) Low temperature feasibility of this reaction make it possible to obtain the thermodynamically unstable isomer IXa-d, if reaction temperatures were well adjusted.

Whether we shall be able to stretch this approach to more complicated systems is of interest in connection with annulene synthesis, which is now in progress in our laboratories.

REFERENCES AND NOTES

* All the new compounds prepared in this communication gave nmr, mass and ir spectra consistent with the assigned structures. New compounds gave satisfactory elemental analyses. Only physical data concerning to IXa, Xa and XIa were described due to the limiting space. Others shall be described in full paper.

Xa, mp 93° (EtOH); separated by column chromatography (SiO₂, benzene) as an earlier fraction, electronic spectrum in EtOH, 237 nm (9,900), 288 (12,900); $\nu_{C=O}$ (KBr) 1690 cm⁻¹; mass spectrum m/e 231 (M⁺); nmr in DMSO-d₆ (100 MHz), Me (1.16, d, J = 7 Hz, 3H), Me (2.20, s, 3H), CH₂ (2.43, m, 1H), CH (2.60, m, 1H), CH₂ (3.00, m, 1H), and benzenoid protons centered at 7.56 and 8.26, 4H. XIa, yellow oil, from the slow moving band; electronic spectrum in EtOH, 219 nm (12,900), 275 (9,900); $\nu_{C=O}$ (neat) 1708 cm⁻¹; mass spectrum m/e 231 (M⁺); nmr in DMSO-d₆ (100 MHz), Me (1.23, d, J = 7 Hz), Me (1.76, s, 3H), CH (2.95, m, 1H), CH (3.42, d, 1H, J = 4 Hz), olefinic proton (7.52, m, 1H), and benzenoid protons centered at 7.52 and 8.17, 4H.

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- † Presumably by the addition of H₂O in stead of HX.

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