

The Synthesis of an Oxygen-bridged Hydroxy[15]annulenone: The Effects of Introducing One Hydroxy Group into the Flexible Segment of a 14 π Perimeter

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Mono-*trans*-hydroxy[15]annulenone (**6**) forms a keto-enol tautomeric mixture with the keto tautomer (**7**) in CH₂Cl₂; (**6**) was rapidly isomerized into the *cis*-enol (**8**) on dissolution in dimethylformamide, dimethyl sulphoxide, and MeOH, indicating that the intramolecular H-bond of (**6**) is easily broken owing to the motional freedom of the segment on which the OH group was introduced.

The influence of introducing intramolecular H-bond(s) into the 14 π perimeter of a higher [4*n* + 3]annulenone (*n* > 3) has not been fully investigated.¹ We have found that 2-hydroxy[15]annulenone (**6**), prepared according to Scheme 1, exists as a keto-enol tautomeric mixture with (**7**) in CH₂Cl₂ and isomerizes very rapidly into the *cis*-enol (**8**) on dissolving the mixture in MeOH [or dimethylformamide (DMF), dimethyl sulphoxide (DMSO)]. Consequently we have obtained (**6**), (**7**), and (**8**) as a 'tautomeric triad.' This result contrasts markedly with our previous finding that position isomeric hydroxy[15]annulenone (**2**)¹ forms a strong intramolecular H-bond and exists only as the enolic form. Our present findings can be well understood by assuming a segmental flexibility increased on the five sp²-carbon loop of (**6**).²

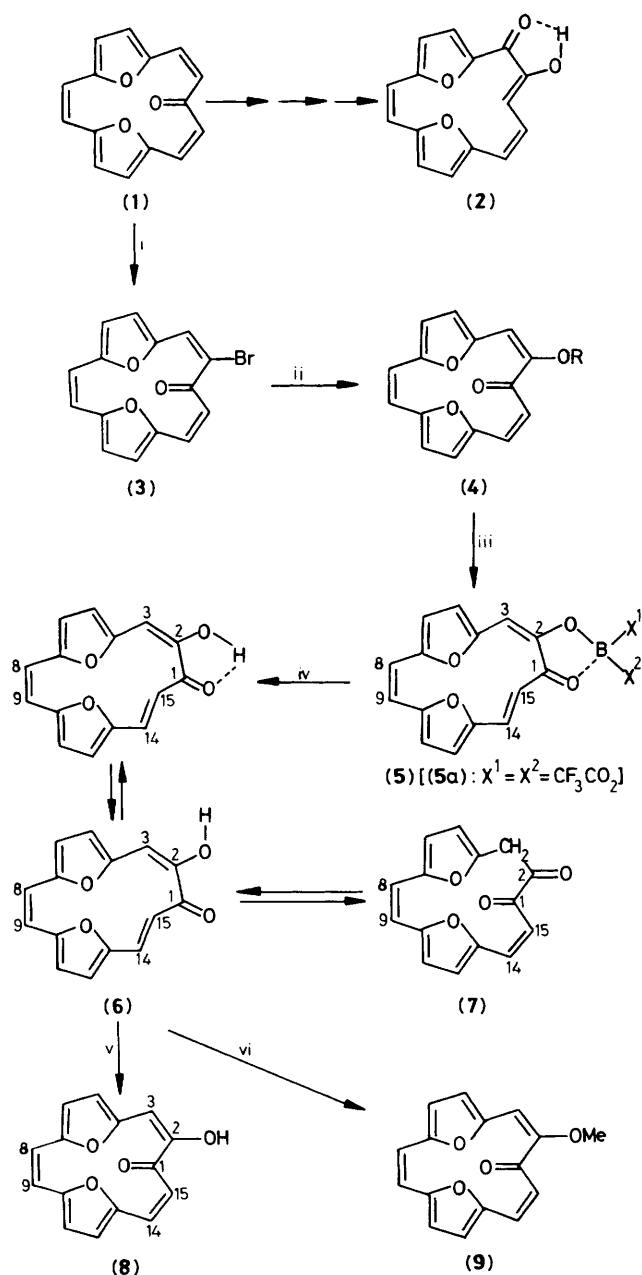
Compound (**1**) was treated with 1.15 mol. equiv. of *N*-bromosuccinimide (NBS) in CH₂Cl₂ to give (**3**) (74%).

Compound (**3**) was treated with 1.3 mol. equiv. of NaOCH₂-CH₂OMe (prepared *in situ*, at room temperature in absolute 2-methoxyethanol). The reaction gave a complex mixture of products from which (**4**) was isolated after chromatographic separation (SiO₂, CH₂Cl₂, 20%). Compound (**4**) was allowed to react for two hours in CF₃CO₂H with 5 mol. equiv. of BBr₃. By applying two different quenching methods to the reaction mixture, we obtained different products. On quenching the reaction mixture in aq. NaHCO₃, a mixture of boron chelates (**5**) possessing different combinations of X¹ and X² (X¹ and X² may be CF₃CO₂ or Br) was obtained. Compound (**5a**) (X¹ = X² = CF₃CO₂) was purified from the mixture by silica gel chromatography [(**5a**): m.p. 239–241 °C (MeNO₂), red needles, 41%; i.r. (KBr) 1770 cm⁻¹ [ν (C=O), ester]; *m/z* 490.02951 (calcd. for C₁₉H₆O₈BF₆, 490.02936)]. The ¹H n.m.r. spectrum of (**5a**) confirmed the structure (Table 1),

Table 1. ¹H N.m.r. spectral data for compounds (**5a**), (**6**), (**7**), and (**8**) (at 23 °C) (*J* values in Hz).

Proton	(5a)	(6)	(7)	(8)
	in [2H ₆]acetone	in CDCl ₃	in CD ₂ Cl ₂	in CD ₃ OD
Furan	9.43, d (<i>J</i> 4.7)	7.80, d (<i>J</i> 4.0)	6.29, d (<i>J</i> 3.3)	6.94, d (<i>J</i> 3.4)
	9.52, d (<i>J</i> 4.7)	7.95, d (<i>J</i> 4.0)	6.41, d (<i>J</i> 3.3)	7.30, d (<i>J</i> 3.4)
	9.57, d (<i>J</i> 4.8)		6.45, d (<i>J</i> 3.5)	7.17, d (<i>J</i> 3.8)
	9.64, d (<i>J</i> 4.8)	7.96, 2H, s	6.58, d (<i>J</i> 3.5)	7.18, d (<i>J</i> 3.8)
H-3	9.57, 1H, s	8.22, 1H, s		6.53, 1H, s
H-8 and -9	9.23, d (<i>J</i> 11.8)	7.66, d (12.4)	6.05, d (<i>J</i> 13.1)	6.84, d (<i>J</i> 13.0)
	9.57, d (<i>J</i> 11.8)	7.87, d (<i>J</i> 12.4)	6.14, d (<i>J</i> 13.1)	6.95, d (<i>J</i> 13.0)
H-14	10.16, d (<i>J</i> 14.0)	8.95, d (<i>J</i> 14.8)	6.25, d (<i>J</i> 12.8)	7.18, d (<i>J</i> 11.1)
H-15	-4.62, d (<i>J</i> 14.0)	1.67, d (<i>J</i> 14.8)	6.73, d (<i>J</i> 12.8)	7.27, d (<i>J</i> 11.1)
OH		ca. 9.0 (at -90 °C, very broad s)		
CH ₂			4.12, 2H, s	

indicating that (5a) is strongly diatropic. On the other hand, the above reaction mixture was quenched in an aq. 0.5% NaOH solution and then acidified with 10% HCl. The CH₂Cl₂ extract of the mixture was purified on a cellulose column (CH₂Cl₂ eluant). The i.r. and ¹H n.m.r. (270 MHz) data of the eluant indicated that it consists of a tautomeric mixture of (6) and (7) [i.r., (6), ν(C=O) (CH₂Cl₂) 1602 cm⁻¹; (7), ν(C=O) (CH₂Cl₂) 1722, 1695 cm⁻¹]; the ¹H n.m.r. data (270 MHz) revealed the following information. The methylene signals of diketone (7) proved to be temperature dependent; it exhibited a broad singlet at δ 4.12 at 23°C, which disappeared at 0°C, and, on further cooling, gave an AB system at δ 4.80 and 3.62 (*J* 15.1 Hz, at -80°C). On the other hand, all the proton signals of (6) became progressively broader on cooling. This indicates that a rapid exchange may take place to form and to



Scheme 1. Reagents and conditions: i, NBS; ii, RONa (R = MeOCH₂CH₂); iii, BBr₃, CF₃CO₂H, then aq. NaHCO₃; iv, aq. NaOH then HCl; v, MeOH (DMF, DMSO); vi, CH₂N₂.

break the intramolecular H-bond. The OH signal of (6) (δ ca. 9.0, † br. s) could not be discriminated until the temperature was down to -90°C.³ The broadening of the enolic proton is probably due to exchange of the enolic protons on different molecules. The proposal that (6) should have one OH group in the perimeter was supported by the finding that 2-methoxy-[15]annulene (9) was obtained when (6) was treated with diazomethane in CH₂Cl₂. The *trans*-enol (6) proved to be diatropic, exhibiting the inner proton at high field and other eight outer protons at low field (Table 1). On cooling, the inner proton resonance caused an appreciable high-field shift with broadening of the signals [d at δ 1.63 with *J* 14.88 Hz (23°C), δ 1.38 (0°C), 1.26 (-10°C), 0.95 (-30°C), 0.54 (-50°C), 0.06 (-70°C), and -0.24 (-80°C)].

The following finding was made on the strength of the intramolecular H-bond of (6). On dissolving (6) in a solvent such as DMF, DMSO, or MeOH, all the proton signals of (6) disappeared almost instantaneously and new signals of the *cis*-enol (8) were developed (Table 1). This indicates that the intramolecular H-bond is easily broken by such solvents.

In summary, our findings described above can be well understood by the following considerations. (i) We have succeeded in isolating the unstable *trans*-enol (6) using the boron chelate (5) as precursor.⁴ The *trans*-enol (6) is strongly diatropic, but it can sustain its geometry only in such a solvent as CH₂Cl₂ or CHCl₃. The H-bond of (6) stabilizes the *trans*-enolic form by developing a 14π Hückel system. However this electronic stabilization is to be balanced with the motional freedom described below. (ii) The OH group introduced at the C-2 position allows an increase in the motional freedom of the loop segment and forces the C-3 centre of (6) to take an sp³-conformation, thus equilibrating ketonization (6) → (7) with enolization (7) → (6). The ratio of (6):(7) is ca. 1:1. (iii) Solvents capable of forming an intermolecular H-bond with (6) can switch off the intramolecular H-bond of (6). This triggers another motion(s), and isomerization (6) → (8) occurs at a rapid rate.

It can be concluded that the strength of the intramolecular hydrogen bond developed on the flexible loop segment of the diepoxy[15]annulene frame is quite dependent on the positions of the C=O and OH groups to be introduced. Therefore, in further work, it is necessary to compare the influence of the OH group substitution in the 2 and 3 positions of the perimeter.

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† If we assume that the proton signal of the chelated OH and the free OH group should appear at δ 15 and 4,⁵ respectively, the observed OH chemical shift of (6) (δ ca. 9.0) shows that the mole fraction of the free OH in (6) is ca. 0.5. This indicates that the chemical shift of the OH proton of (6) should be an average of the shifts of these two structural forms.