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Conference Paper

Construction of a [15]Annulenone-[15]annulenyl Ion Cycle*

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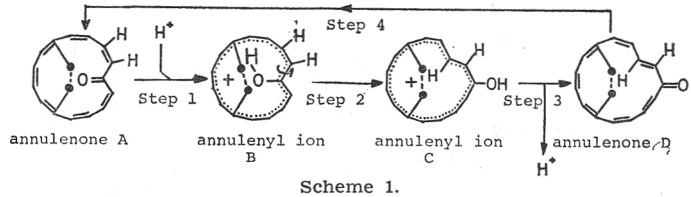
Previously, we have reported the synthesis of furanoid [15]annulenones and their protonated species. With the benefits of FT NMR spectroscopy, some of experiments have now been reinvestigated.

The annulenone may undergo dynamic conformational changes to provide an interesting cycle, which can be driven by protonation--deprotonation sequence.

From the biochemical point of view, [4n+3]annulenones[1] are more interesting chemical species than homologous [4n+2]annulenes, because they can accept H^+ from the external milieu to form aromatic [4n+3]annulenyl ions. If we construct an annulenone A (see Scheme 1), whose structure is specified as described below, it may undergo dynamic conformational changes according to the general scheme thus providing an interesting cycle, which can be driven by the protonation-deprotonation sequence.[2]



Scheme 1.

The cycle can be described in terms of four subsequent reactions. The carbonyl group of annulenone A to be protonated is placed inside of the ring with internal bridging group(s). Annulenyl ion B formed by step 1 triggers off the movement of the inside OH group to the outside positions of the ring by the pseudorotation of the C···C bond, as depicted in step 2. The resulting isomeric annulenyl ion C is then deprotonated to provide a less stable annulenone D, which contains one inner hydrogen. The geometrical properties of

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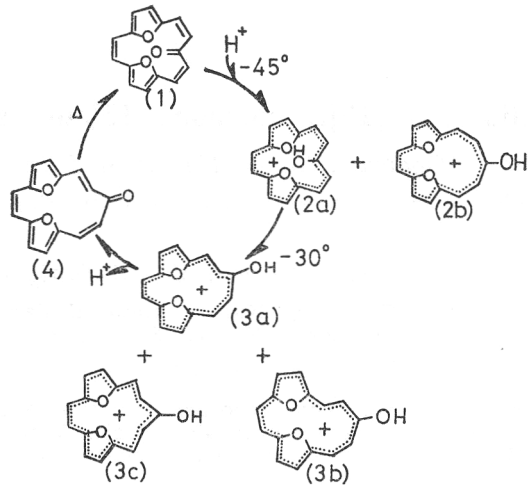
annulenone D (angle strain, loss of symmetry, and the presence of one inner proton) would result in its isomerization to regenerate annulenone A in step 4.

We demonstrate here the first successful application of this principle by using oxygen-bridged [15]annulenone (1) (see Scheme 2)[3].



Scheme 2 The [15]Annulenone-[15]Annulenyl Ion Cycle

The first step of the cycle is the protonation of [15]annulenone (1) (for ^{1}H and ^{13}C NMR spectra, see Figure 1.). This process usually gave an equili-

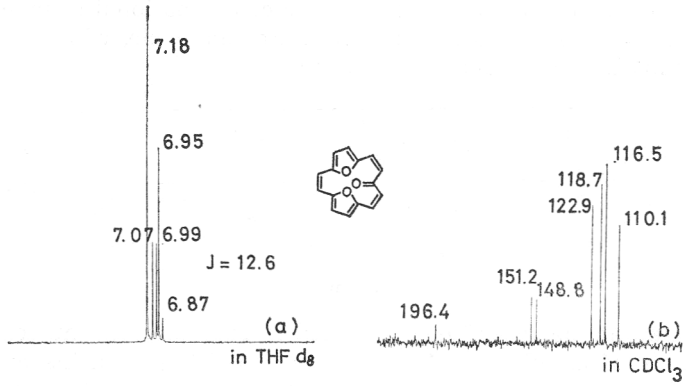


Fig. 1. ^{1}H and ^{13}C nmr spectra of [15]annulenone (1)

brium mixture of isomeric annulenyl ions, whose structures and compositions depend entirely upon the protonation condition used. The annulenyl ion (2a) could be obtained only at extremly low temperature (in CD_2Cl_2, below at —45 °C). At room temperature a two component equilibrium mixture consisting of 83% (3a) and 17% (2b)[4] was obtained in CF_3COOD (^{1}H NMR). In turn, similar protonation at —20 °C with CF_3COOD + CD_2Cl_2 gave a three component

mixture (see Figure 2.). In this case the annulenyl ion (3a) was again obtained as an abundant isomer. The minor products were posturated to have structure (3b) and (3c), which differ from (3a) only in the position and the number of the inner hydrogen(s). This proposal is based on the finding that the NMR spectrum of the mixture exhibited three pairs of highfield doublets attributable to the respective inner proton of these isomers at δ — 4.3 ~ —4.5 (Figure 2.).

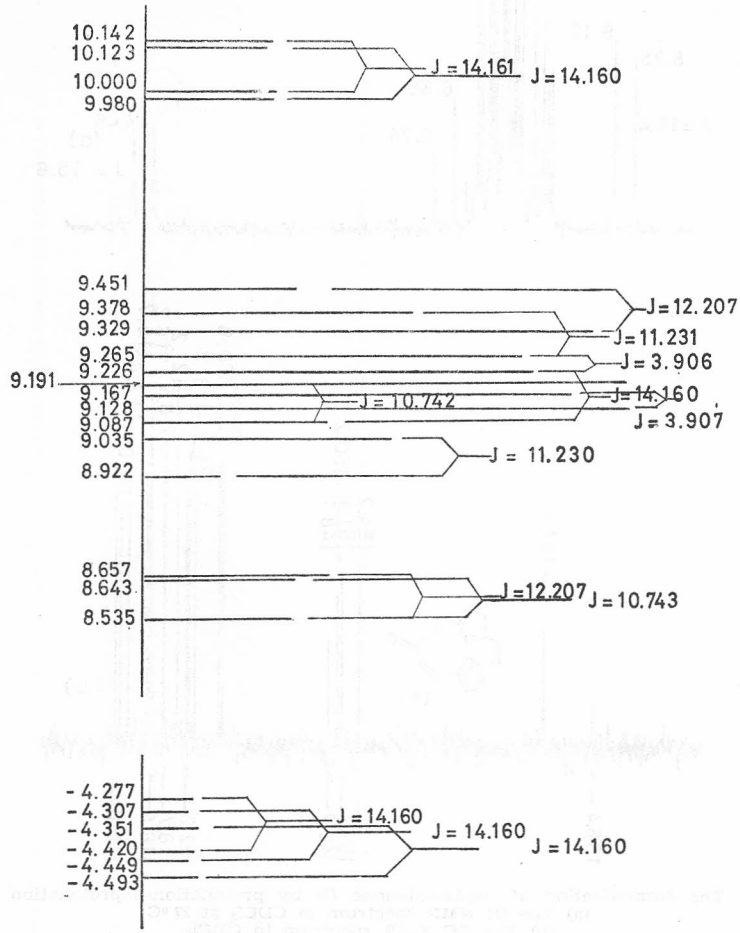


Figure 2. The ^1H NMR spectrum of the protonation products of annulenone (1) at — 20 °C in CD_2Cl_2 with CF_3COOD.

From these results the following inferences can be drawn. Firstly, conformational change (2a) → (3a) is extremely fast at room temperature, and this isomerization can be retarded only at very low temperature. Secondly, at low temperature (at — 20 °C) at least three possible trans annulenyl ions are capable of existance. Among them the annulenyl ion (3a) exists as a thermodynamic sink. This can be explained well by the consideration that two C$^{\cdots}$C bonds attached to each rotatable trans C$^{\cdots}$C bond are almost parallel to each other in the pentadecagon periphery of (2a)[5], thereby rendering

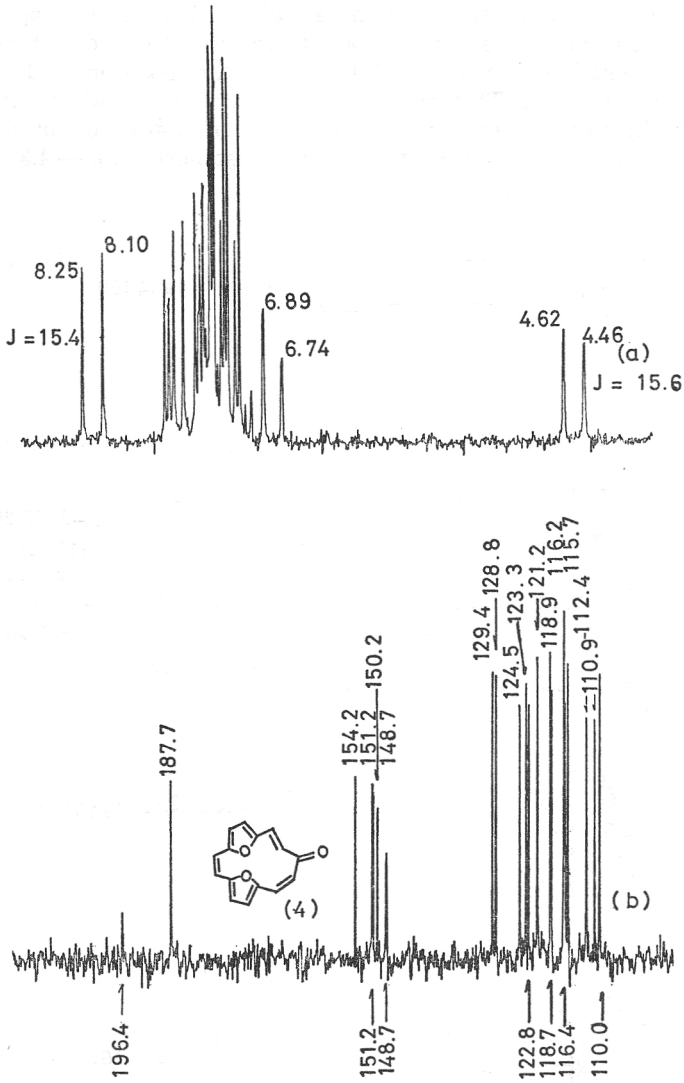


Figure 3. The Isomerization of (15)Annulenone (1) by protonation-deprotonation sequence
(a) The ^{1}H NMR spectrum in $CDCl_3$ at 27 °C
(b) The ^{13}C NMR spectrum in $CDCl_3$
Signals described in the lower part of the ^{13}C NMR spectrum in (b) are ascribable to those of (I).

trans C⋯⋯C bond(s) more susceptible to rotation. Thirdly, a distinct pk_a difference (Δpk_a) can be produced by the cycle between the annulenyl ion (2a) and (3a)[6,7].

Annulenone (4) could be obtained by the quenching of (3a) into ice-cold 5% aq. K_2CO_3 solution. The ^{1}H and ^{13}C NMR spectra of (4) confirmed the structure (see Figure 3(a) — 3(c)). The observed upfield shift of the inner proton (δ 4.53, d, $J = 16$ Hz) relative to the outer ones (δ 6.83 — 8.18) indicated that annulenone (4) is clearly diatropic. On dissolving (4) into CD_3OD, the inner

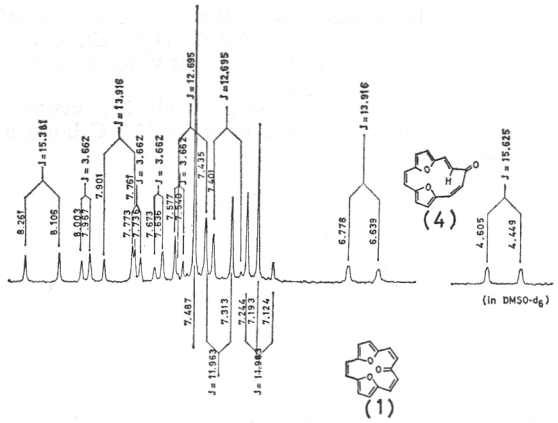


Figure 3(c)
(c) The ^{1}H NMR spectrum of the deprotonated products measured in DMSO-d_6 at 25 °C (100 MHz).

proton signals were shifted to a greater extent upfield, exhibiting 1H doublet at δ 1.28 (J = 15 Hz) at —50 °C. This shift indicates that the dipolar form of (4) was increased in the protic solvent.

The final step of the cycle is the thermal isomerization of (4) into (1). We observed that the rate of the isomerization was very rapid at room temperature, if a trace of H^+ was presented. In contrast, the thermal process requires rather high temperature in DMSO-d_6 and proceeds with a much slower rate ($k_{70\,°C} = 0.024$ min^{-1}, NMR spectroscopy), indicating that the decreased rate is reflective of the decreased π-delocalization.

To summarized the following remarks can be made.

1. The [15]annulenone-[15]annulenyl ion cycle described above can produce two high energy compounds (2a) and (4) by protonationdeprotonation sequence. Stable geometries are reversed in the respective charged and uncharged species [i. e., annulenone (1) is more stable than annulenone (4), whereas annulenyl ion (3a) is more stable than annulenyl ion (2a)].

2. The delocalized aromatic 14π system plays a crucial role in the dynamic conformational changes in both species, because such facile geometrical isomerization observed are accessible only in well developed π-systems.

3. The carbonyl carbon of (1) may be regarded as an »active center«, where a change of acid-base properties of the annulenyl ion species could be induced. The two oxygen atoms incorporated in the 15-membered ring not only serve as internal bridges, but they also facilitate the above isomerization by means of their suitable sterical hindrances imposed on the ring.

Further quantitative studies are needed in order to elucidate the overall energetics of the cycle. Efforts along this line are now in progress.

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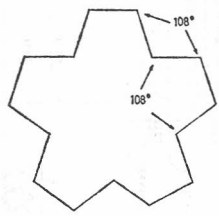
4. The existance of (2b) could be recognized by the careful studies of the NMR spectra in the titration experiments of (1) with CF_3COOD in CD_2Cl_2 (H. O g a w a et al., unpublished results). At room temperature annulenyl ion (2b) exists as an essentially nonmobile isomer in the solvent system.
5. In the D_{5h} geometry of regular pentadecagon, all the inside and outside bond angles become equal (108°), and each pair of the C⋯⋯C bond attached to a rotatable C⋯⋯C bond is parallel.



6. Both pk_a of (2a) and (3a) were measured at very low temperature.
   As we observed, at room temperature isomerization (2a) → (3a) occurrs so rapidly that the equilibrium (2a) ⇄ (1) + H^+ is never really established. At — 40 °C, the above isomerization was negligible in Cd_3OD. Therefore, according to the following procedure, the pk_a of (2a) was measured at — 40 °C. Constant volumes of CF_3COOD were added to a CD_3OD solution of (1) through a digital volumeter. The observed lowfield shift of the NMR signals owing to the formation of (2a) were plotted with moles of acid added. A smooth titration-type curve was obtained, from which the pk_a of (2a) was obtained as — 0.95. There was some difficulties in the measurement of the pk_a of (3a). In this case, protonation occurred concurrently with acid catalyzed isomerization (4) → (1). This isomerization was retarded considerably at — 40 °C. Similar titration of (4) gave a smooth titration-type curve by plotting the observed upfield shifts of the inner proton resonances owing to the conjugated acid (3a) with acid moles. Thus, we obtained + 0.97 as the pk_a of (3a).
   We obtained 1.9 as Δpk_a between annulenyl ion (3a) and (2a).
7. It is of interest to compare the Δpk_a obtained in footnote 6) with these values of a real biological proton pump cycle of purple membrane (bacteriorhodopsin). The size of the pH gradient, produced by the model experiments amounts to several pH units; [for example, $\Delta pH = 2.55$, Y. K a g a w a, K. O h n o, M. Y o s h i d a, Y. T a k e u c h i, and N. S o n e, *Fed. Proc.* **36** (1979) 1815; S. B. H w a n g and W. S t o e c k e n i u s, *J. Membrane Biol.* **33** (1977) 325].

SAŽETAK

Konstrukcija ciklusa [15]anulenon- [15]anulenil-ion

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Eksperimenti izvršeni na ranije sintetiziranim furanoid [15]anulenonima i njihovim protoniranim vrstama preispitani su korištenjem FT NMR spektroskopije.

Podvrgne li se anulenon dinamičkim konformacijskim promjenama, koje prvo protoniranjem daju anulenil-ion, zatim njegov izomer, da bi se deprotoniranjem dobio anulenon s unutrašnjim vodikom, koji izomerizacijom konačno daje početni anulenon, mogao bi se dobiti zanimljiv ciklus u kojemu bi se slobodna energija dobivala na račun protoniranja i deprotoniranja.

Taj je ciklus od posebnog interesa u svezi s stvarnim biološkim ciklusom, ciklusom protonske crpke kod bakteriorodopsina.

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