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SYNTHESIS OF [15]ANNULENONE 4,7:10,13-DIOXIDE DERIVATIVES AND THE DEMONSTRATION OF A DIAMAGNETIC RING CURRENT

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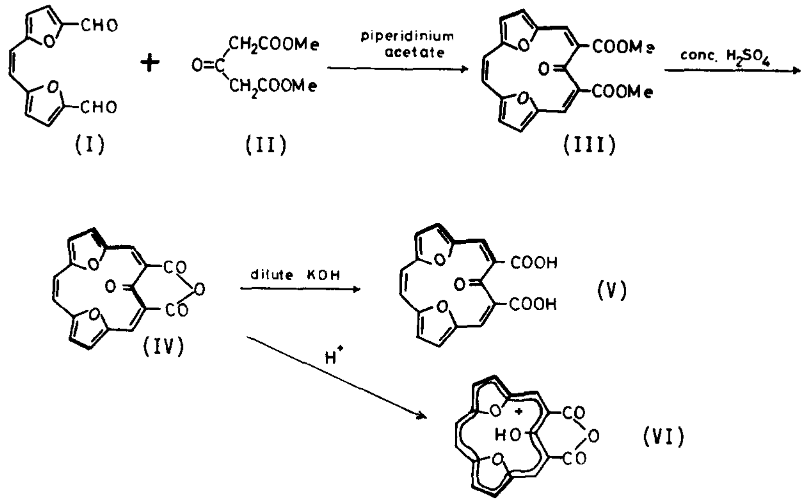
THE name "annulenone„ 1) was given to a fully conjugated monocyclic ketone made up of alternating single bonds and double bonds by G.M.Pilling and F.Sondheimer. These compounds are potentially of interest, because they are considered to be aromatic, provided they contain a coplanar (4n+3)-membered carbon skelton, and provided they sustain a diamagnetic ring current as a consequence of π electron delocalization in an applied magnetic field.

In continuation of our program in establishing methods for the synthesis of (4n+3)-membered heteroannulenone 2) by simple aldol type reaction of dialdehyde with acetonedicarboxylate, we now report on some recent experiments, which have led to some derivatives of [15]annulenone 4,7:10,13-dioxide (III-V), and show the demonstration of an appreciable diamagnetic ring current in



the pmr spectrum of 4,7:10,13-dioxido[15]annulenone 2,15-dicarboxylic acid anhydride (IV). At present, tetramethylene-tetrahydro[15]annulenone,3) a conjugated cyclic enynketone derivative, is only one example of [15]annulenone.

The condensation of cis-α,β-di(5-formyl-2-furyl)ethylene (I) with methyl acetonedicarboxylate (II) in $CHCl_3$ in the presence of piperidinium acetate and the repeated purification by chromatography on silica gel with $CHCl_3$ afforded 2,15-dicarbomethoxy[15]annulenone 4,7:10,13-dioxide (III) in 20 % yield, mp 170° (red prisms); UV λ_{max}^{MeOH} mu 271 (ε 24800), 334 (27400) and 450 (5050); ν_{max}^{Nujol} cm^{-1} : 1713 (ν c=o ester), 1660 (ν c=o ketone), 1613 (ν c=c); mass spectrum, molecular ion at m/e 354. The pmr spectrum of (III) confirmed the structure. The 6H singlet at δ 3.82 was assigned to the carbomethoxy protons, the 2H two doublets centered at δ 6.96 and 7.19 with J = 4 Hz to the furan protons, the two 2H singlets at δ 6.70 and 7.73 to the olefinic protons.

On standing this diester (III) with excess of H_2SO_4 for 1 day at room temperature, followed by quenching the solution on ice gave the corresponding anhydride (IV) in an almost quantitative yield. Substance (IV) was a dark red crystalline substance, mp 360° (from CH_3CN); UV λ_{max}^{MeCN} mu 260 (24200), 355 (36000), 490-500 (6580) and 520 (7700); ν_{max}^{KBr} cm^{-1} : 1733, 1700 (ν c=o anhydride), 1688 (ν c=o ketone); mass spectrum, molecular ion at m/e 308; pmr spectrum, the 2H singlet at δ 7.75, another 2H singlet at δ 8.57, the 4H two doublets each centered at δ 8.00 and 8.35 with J = 4 Hz due to the furan protons.

Treatment of (IV) with dilute KOH solution at room temperature and the subsequent acidification of the solution with dilute HCl yielded the corresponding dicarboxylic acid (V) without apparent loss; beautiful black prisms (from ethyl acetate), decomp at 300° without melting; UV λ_{max}^{MeCN} mu 248 (36200), 256 (45200), 267 (44700), 330 (27000) and a subsidiary peak at 450 mu (4600); ν_{max}^{KBr} cm^{-1}: 1680, 1713 (ν c=o carboxylic acid), 1660 (ν c=o ketone); pmr spectrum in d_6-dimethylsulfoxide showed the 2H singlet at δ 6.86, the 2H singlet at 7.69, two doublets due to the furan protons each centered at δ 7.23 and 7.50 with J = 4 Hz and 2H broad signal due to the COOH protons at δ 12.91, which were exchangeable with D_2O. The direct hydrolysis of (III) by the use of dilute KOH was found to give a very poor yield of (V). Facile cyclization of the diester (III) or the dicarboxylic acid (V) into the corresponding anhydride (IV) gave clear chemical evidence that the ketone $\rangle$c=o locates at the inside of the fully conjugated skelton.

On inspection of the molecular models, (III), (IV) and (V) are expected to be almost coplanar π electron systems. However, it is noteworthy to know that the anhydride (IV) is best favoured for catching a coplanarity among them, because (III) and (V) suffer from the disadvantage that the two bulky groups [carbomethoxy groups in (III) or carboxyl groups in (V)] sterically interfer with each other, and thus impose a noncoplanar strained geometry on the skelton. The finding that all olefinic protons of the anhydride (IV) exhibited the corresponding signals at an appreciablly lowered field, whereas all the olefinic protons of (III) or (V) exhibited the corresponding signals at the position where ordinary polyenones resonate, is well agreement with the above consideration.** Therefore, anhydride (IV) is reasonably be concluded to sustain an appreciable diamagnetic ring current in its ground state.

As expected, the diamagnetic ring current was increased when (IV) was protonated. Thus, when (IV) was dissolved in CF_3COOH all olefinic proton signals shifted to down field dramatically and gave rise to two 2H singlets at δ 8.42 and 9.27 (olefinic protons) and to an AB system centered at δ 8.43 and 8.78 with J = 4 Hz (furan protons) [see FIG. 1].

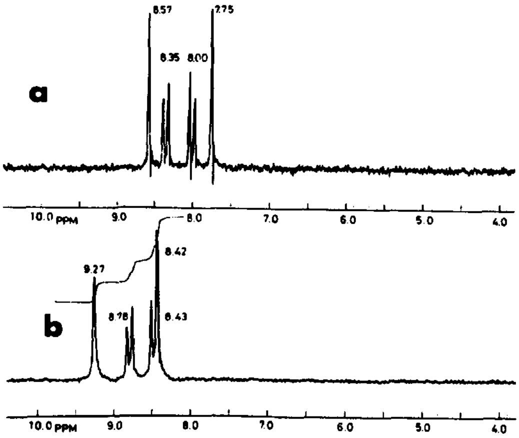


FIG. 1. Pmr spectra of 4,7:10,13-dioxido[15]-annulenone 2,15-dicarboxylic acid anhydride (IV) in d_6-DMSO (a) and in CF_3COOH (b) at 60 MHz.

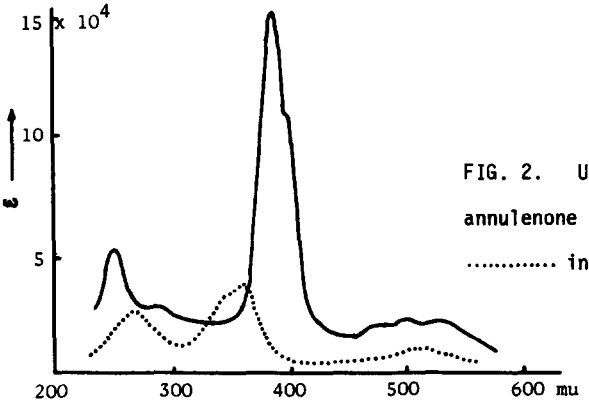


FIG. 2. Uv spectra of 4,7:10,13-dioxido[15]-annulenone 2,15-dicarboxylic acid anhydride (IV) .... in CH_3CN and ——— in H_2SO_4.

Similarly, the pmr spectrum of (III) in CF_3COOH showed also downfield shifts of all olefinic proton signals, i.e., the 6H singlet at δ 4.10 (carbomethoxy protons), the 2H sharp singlet at δ 7.62, and another 2H singlet at δ 8.52 (olefinic protons), and 4H quartet centered at δ 7.83 and 8.10 with J = 4 Hz (furan protons).

The most noticiable and common character of these [15]annulenones obtained here are deep colour developement, when they were dissolved in some strong acid. On dissolving (III), (IV), and (V) in conc. H_2SO_4, beautiful navy blue, red, and blue colour were developed, respectively. These colour developement is well explained by the expected formation of the corresponding 1-hydroxycyclopentadecaheptaenylium cation. Among them, the solution of cation (VI), produced from (V) in H_2SO_4 was found to be particularly stable at room temperature, showing prominent peaks at 383 mu (154000), 392.5 (112000) together with subsidiary peaks at 243 mu (51000), 485 (17600), 500 (16000) and 520 (16600) [see FIG.2].

An effort to obtain free [15]annulenone 4,7:10,13-dioxide [two conformers may be possible] by the decarboxylation of (V) is in progress.

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References

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** The olefinic protons of cis-α,β-di(5-formyl-2-furyl)ethylene in $CDCl_3$ appeared at δ 6.50 as a singlet.[4)]

*** All compounds had satisfactory analyses for proposed structures.

1) G.M.Pilling and F.Sondheimer, J. Amer. Chem. Soc., 90, 5610 (1968); G.W.Brown and F.Sondheimer, ibid, 91, 760 (1969): W.Grimme, J.Reisdorff, W.Jünemann and E.Vogel, J. Amer. Chem. Soc., 92, 6335 (1970).

2) H.Ogawa, H.Kato and M.Yoshida, Tetrahedron Letters, in press.

3) G.P.Cotterrell, G.H.Mitchell, F.Sondheimer and G.M.Pilling, J. Amer. Chem. Soc., 93, 259 (1971).

4) H.Saikachi, H.Ogawa and K.Sato, Chem. Pharm. Bull (Tokyo), 19, 71 (1971).