

A Simple Methodology for Aza-annulene Synthesis: Preparation and Properties of 2,15-Diethoxycarbonyl-4,7 : 10,13-diepoxy-2-cis,8-cis,14-cis-aza[15]annulene

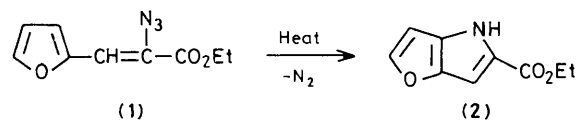
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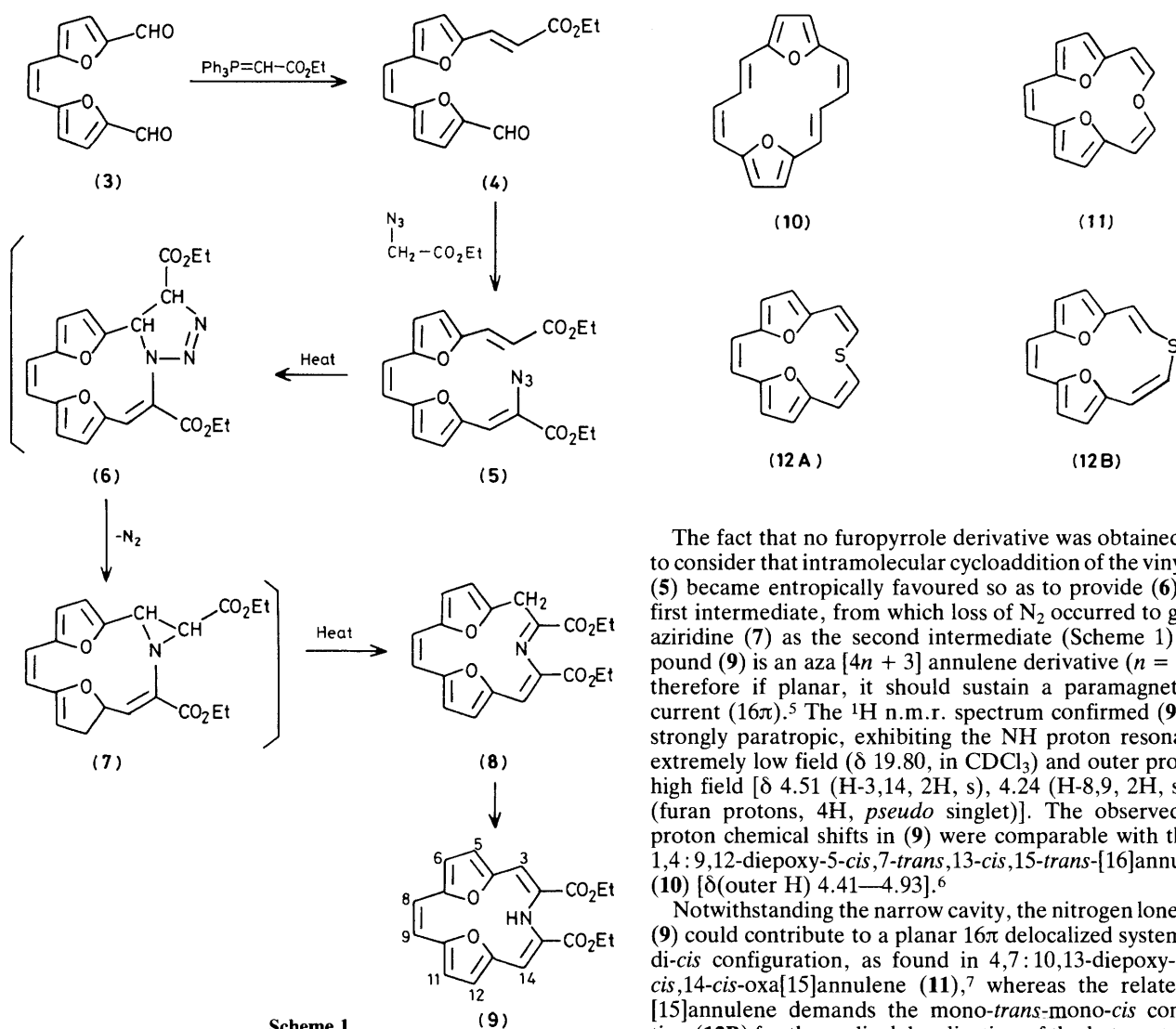
The synthesis and properties of the titled compound (**9**) are described; (**9**) was prepared by the thermolysis of the vinyl azide (**5**) in 70% yield, and no furopyrrole derivatives were formed.

A variety of aza-annulenes have been prepared by a nitrene insertion-ring expansion reaction,¹ since 1*H*-azepine was obtained as the first example by reacting (ethoxycarbonyl)nitrene with benzene.² However, this approach is of limited value, when applied to large ring size annulenes, because nitrene addition occurs nonspecifically in position(s) to give a barely separable mixture of products. We describe here a successful transformation of the dialdehyde (**3**)³ to the aza-annulene (**9**) *via* the thermolysis of the vinyl azide (**5**). Contrary to the fact that the azide (**1**) provides the furopyrrole (**2**) on heating,⁴ (**5**) was readily converted into the aza-



annulene (**9**) without the corresponding furopyrrole derivative being formed. The present method is the first example showing that an NH group can be introduced at a specific position of a medium ring size aza-annulene.

The aldehyde (**4**), readily available by the Wittig reaction of the dialdehyde (**3**)³ with (ethoxycarbonyl)methylenetri-



phenylphosphorane (1 mol equiv.) in 35% yield (m.p. 89–90°C), was condensed with ethyl azidoacetate (3 mol equiv.) in EtOH at room temperature using NaOEt as the base to give the vinyl azide (5) [m.p. 102–104°C (EtOH), 42% yield]. Thermolysis of (5) was conducted at 95°C in *p*-xylene for 3 h, and the product was chromatographed on a column (SiO₂, CH₂Cl₂). An intense blue band developed, from which (9) was obtained as deep blue plates [m.p. 145–147°C (EtOH), 70% yield, *m/z* 369 (*M*⁺), u.v. (EtOH) λ_{max} nm (ε dm³ mol⁻¹ cm⁻¹): 217 (19 000), 249 (25 000), 292 (75 900), 307sh (41 700), 370 (7 900), and 566 (340)].

In order to study the mechanism, the thermolysis was investigated at 75°C in (²H₈)toluene and the progress of the reaction was monitored by ¹H n.m.r. spectroscopy. This revealed that i, after 300 min (5) was completely transformed into the unconjugated species (8), which was capable of existence only as a transient intermediate under the reaction conditions and was tautomerized into (9) over a period of 100 min; ii, compound (8) could be isolated as a yellow oil [λ_{max} (EtOH) nm (ε dm³ mol⁻¹ cm⁻¹): 290 (21 500) and 430 (9 800)], when the thermolysis mixture was chromatographed at 2°C in the dark (SiO₂, CH₂Cl₂).†

† The structure of (8) was confirmed by spectral data and by elemental analysis. The ¹H and ¹³C n.m.r. signals of the ring CH₂ group appeared at δ 4.38 (2H, s) and 35.63 p.p.m., respectively.

The fact that no furopyrrole derivative was obtained led us to consider that intramolecular cycloaddition of the vinyl azide (5) became entropically favoured so as to provide (6) as the first intermediate, from which loss of N₂ occurred to give the aziridine (7) as the second intermediate (Scheme 1). Compound (9) is an aza [4*n* + 3] annulene derivative (*n* = 3), and therefore if planar, it should sustain a paramagnetic ring current (16π).⁵ The ¹H n.m.r. spectrum confirmed (9) to be strongly paratropic, exhibiting the NH proton resonance at extremely low field (δ 19.80, in CDCl₃) and outer protons at high field [δ 4.51 (H-3,14, 2H, s), 4.24 (H-8,9, 2H, s), 5.06 (furan protons, 4H, *pseudo* singlet)]. The observed outer proton chemical shifts in (9) were comparable with those of 1,4:9,12-diepoxy-5-*cis*,7-*trans*,13-*cis*,15-*trans*-[16]annulene (10) [δ(outer H) 4.41–4.93].⁶

Notwithstanding the narrow cavity, the nitrogen lone pair of (9) could contribute to a planar 16π delocalized system in the di-*cis* configuration, as found in 4,7:10,13-diepoxy-2-*cis*,8-*cis*,14-*cis*-oxa[15]annulene (11),⁷ whereas the related thia-[15]annulene demands the mono-*trans*-mono-*cis* configuration (12B) for the cyclic delocalization of the heteroatom lone pair instead of the di-*cis* configuration (12A).⁸ Finally, it should be mentioned that the observed isomerization (8)→(9) was reversible, compared with the 1*H*- → 3*H*-azepine tautomerization, in which 3*H*-azepine becomes favourable on standing.⁹

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References

- G. Schröder, *Pure Appl. Chem.*, 1975, **44**, 925; A. G. Anastassiou, *ibid.*, p. 691.
- K. Hafner, *Angew. Chem.*, 1963, **75**, 1041; *Angew. Chem., Int. Ed. Engl.*, 1964, **3**, 165.
- H. Saikachi, H. Ogawa, and K. Sato, *Chem. Pharm. Bull.*, 1971, **19**, 97.
- H. Hemetsberger and D. Knittel, *Monatsh. Chem.*, 1972, **103**, 194.
- F. Sondheimer, *Acc. Chem. Res.*, 1972, **5**, 81.
- H. Ogawa, C. Fukuda, T. Imoto, I. Miyamoto, H. Kato, and Y. Taniguchi, *Angew. Chem.*, 1983, **95**, 412; *Angew. Chem., Int. Ed. Engl.*, 1983, **22**, 417; *Angew. Chem. Suppl.*, 1983, 480.
- H. Ogawa and M. Kubo, *Tetrahedron Lett.*, 1971, 4859.
- H. Ogawa, T. Imoto, I. Miyamoto, Y. Taniguchi, T. Koga, and Y. Nogami, *Heterocycles*, 1982, **19**, 2047.
- E. Vogel, H.-J. Altenbach, J.-M. Drossard, H. Schmickler, and H. Stegelmeier, *Angew. Chem.*, 1980, **92**, 1053; *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 1016.