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A NEW XYLYLENE-LIKE INTERMEDIATE: 2-ALLYLIDENE-5-METHYLENE-2,5-DIHYDROFURAN. SYNTHESIS OF [6.2], [4.4], and [4.2]FURANOPHANES.

S. H. Küsefoglu and Daniel T. Longone*
Department of Chemistry, The University of Michigan,
Ann Arbor, Michigan 48109

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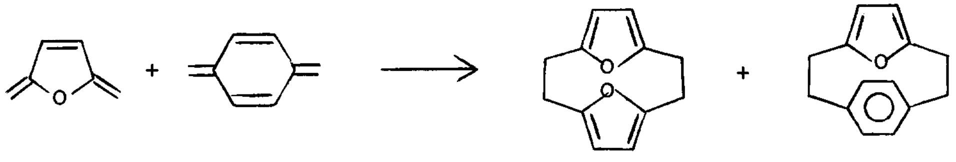
The reactive species 2,5-dimethylene-2,5-dihydrofuran (**1**) is a valuable intermediate for the synthesis of bridged-aromatic compounds. Generated conveniently[1] by a 1,6-Hofmann elimination, **1** dimerizes or cross-dimerizes with other xylylene-like species (e.g., *p*-xylylene, **2**) to give phanes[2] containing a bridged furan ring (e.g., **3** and **4**). The furan unit is particularly useful as it provides a functionality for structural transformations within the macrocyclic system. The syntheses, structural properties, and chemical transformations of phanes of type **3** and **4** are of continuing interest.[3] As useful as **1** is, it necessarily provides bridged-aromatic structures containing solely two-carbon bridges. We describe here the synthesis and characterization of a vinylog of **1**, 2-allylidene-5-methylene-2,5-dihydrofuran (**6**). Compound **6**, easily prepared by a 1,8-Hofmann elimination,[4] provides a macrocycle unit for the construction of functionalized [6.2], [4.4], and [4.2]phane systems, thereby making accessible structures which have been either unknown or difficult to prepare by alternate routes.

Reductive amination[5] of 5-methylfuran-2-acrolein[6] (**5a**) with DMF/HCOOH gives the tertiary amine **5b**. Methylation and anion exchange in the usual manner[7] provides the quaternary ammonium hydroxide **5c**. Pyrolysis of **5c** (as a moist semi-solid) at 80-100° and 0.5 mm pressure occurs smoothly to give the 1,8-elimination product **6**, isolated in a cold trap.[8] Thus obtained (70% yield), **6** is a yellow liquid of moderate stability: it can be kept for weeks in a freezer, under nitrogen; as a 10% solution in CCl_4 it has a half-life of about 90 min at room temperature. The NMR spectrum of **6** is summarized below (60 MHz, $CDCl_3$); MS, m/e 120 (100%, M^+), 91 (96%), 65 (21%), and 39 (32%).



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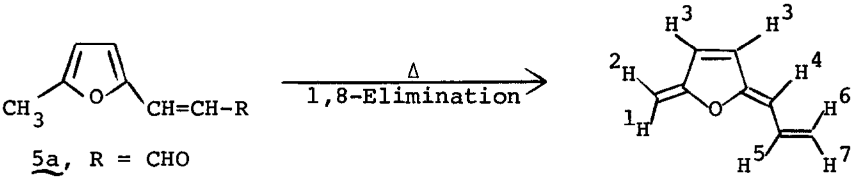


6

5a, R = CHO
b, R = CH_2NMe_2
c, R = $CH_2\overset{+}{N}Me_3\overset{-}{O}H$

NMR (δ):
H^1 = 4.25 (d, J 1.8)
H^2 = 4.60 (d, J 1.8)
H^3 = 6.43 (s)
H^4 = 6.0 (m)
H^5 = 5.4 (m)
$H^{6,7}$ = 5.0-5.2 (m)

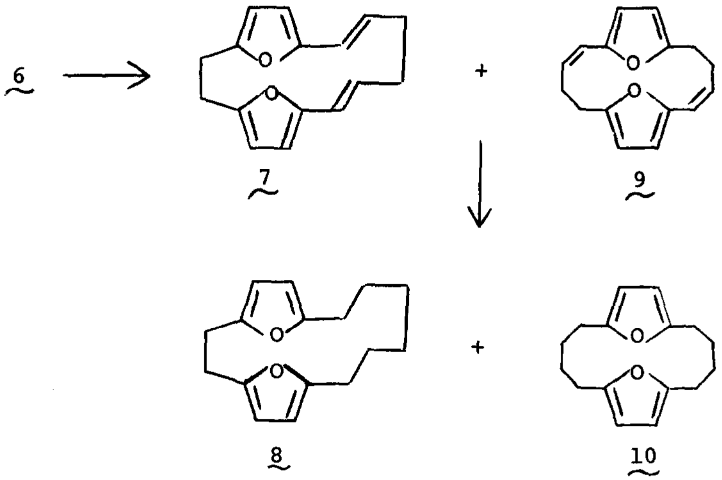
When the Hofmann base 5c is pyrolyzed in water/toluene,[1] it affords mainly the head-to-head, 1,8-to-1,8 dimer of 6, [6.2](2,5)furanophane-1,5-diene[2] (7) in 33% yield.[9] Dimer 7 has mp 84-85° (MeOH). ^{1}H-NMR (CCl_4): δ 6.0 (AB, 4H, furan); 5.8 (m, 4H, vinyl); 2.8 (s, 4H, [2]-bridge methylenes); and 2.4 (m, 4H, [6]-bridge methylenes). MS, m/e 240 (100%, M^+), 120 (86%), and 91 (48%).[10] The bridge double bonds are assigned the trans-configuration as shown based on the IR spectrum (KBr): 1680 (m) and 970 (s) cm^{-1}.

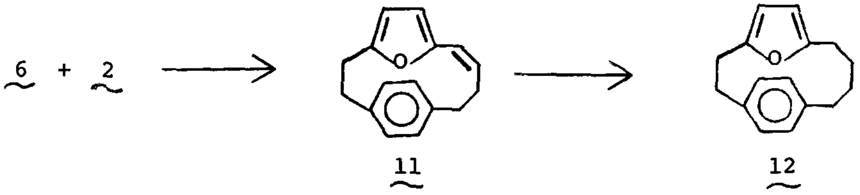
The α,β-unsaturated furan moiety in 7 is somewhat air sensitive and the [6.2] system is best preserved in its reduced form. Hydrogenation of 7 (Pd/C) gives [6.2](2,5)furanophane (8)[10] in 83% yield: mp ($MeOH-H_2O$) 8-9°; ^{1}H-NMR, δ 5.8 (AB,4H, furan), 2.9 (s, 4H, [2]-bridge methylenes), 2.6 (m, 4H), 1.6 (m, 4H), and 1.4 (m, 4H); MS, m/e 244 (100%, M^+), 201 (36%), 119 (91%), 117 (91%), and 107 (82%).

Pyrolysis of 5c provides, in addition to 7, the head-to-tail system[11] 9, best isolated as 10 by hydrogenating the pyrolysis product mixture, followed by TLC separation (6% yield). Product 10, [4.4](2,5)furanophane,[10] has: mp (MeOH) 143-143.2°; NMR, δ 5.8 (s, 4H, furan), 2.6 (m, 8H), and 1.5 (m, 8H); MS, m/e 244 (100%, M^+), 187 (12%), 173 (11%), 147 (15%) and 107 (20%).

Compound 10, to our knowledge, is the first example of a [4.4]furanophane; the [6.2]furanophane system has been generated previously by two methods of less general synthetic utility.[12]

The usefulness of 6 in phane syntheses has been extended by cross-dimerization. Pyrolysis in water/toluene of an equimolar mixture of 5c and the Hofmann base precursor[1] of 2 provides, in addition to the expected homo-dimers, the mixed system 11. As in the cases above, the [4.2] system is best





isolated and purified as the dihydro derivative. The pyrolysis product mixture was hydrogenated and subsequent TLC separation gave [4]paracyclo[2](2,5)-furanophane (12)[13] in 13% yield.[10] Product 12 has: mp (MeOH) 76-77°; ^{1}H-NMR (CCl_4), δ 6.8 (s, 4H, benzenoid), 5.6 (AB, 2H, furan), 2.68 (m, 4H, [2]-bridge methylenes), 2.5 (m, 2H), 2.2 (m, 2H), and 1.6 (m, 4H); MS, m/e 226 (73%, M^+), 198 (33%), and 104 (100%).

The new structures reported here are of intrinsic interest as higher homologs of the extensively studied [2.2] systems. In addition, we believe that they will prove useful intermediates in the broader field of macrocyclic chemistry. Compounds 8 and 10, for example, are essentially C_{16} *bis*-(1,4-diketones). Functional group transformations in these compounds as well as other cyclization reactions of 6 are subjects of current study.

REFERENCES AND NOTES

1. H. E. Winberg, F. S. Fawcett, W. R. Mochel and C. W. Theobald, *J. Am. Chem. Soc.*, **82**, 1428 (1960).
2. For phane nomenclature see: B. H. Smith, "Bridged Aromatic Compounds," Academic Press, New York, 1964; F. Vögtle and P. Neumann, *Tetrahedron*, **26**, 5847 (1970); K. Hirayama, *Tetrahedron Lett.*, 2109 (1972).

3. For recent reviews see: G. R. Newkome, J. D. Sauer, J. M. Roper and D. C. Hager, *Chem. Rev.*, **77**, 513 (1977); F. Vögtle and P. Neumann, *Topics in Current Chemistry*, **48**, 67 (1974); F. Vögtle and P. Neumann, *Synthesis*, 85 (1973). See also: M. Nakazaki, K. Yamamoto, and S. Tanaka, *J. Org. Chem.*, **41**, 4081 (1976); T. Otsubo, S. Mizogami, N. Osaka, Y. Sakata, and S. Misumi, *Bull. Chem. Soc. Jap.*, **50**, 1841, 1858 (1977).
4. L. G. Kaufman and D. T. Longone, *Tetrahedron Lett.*, 3229 (1974). A second example of a synthetically useful 1,8-Hofmann elimination has been described: R. Luhowy and P. M. Keehn, *J. Am. Chem. Soc.*, **99**, 3797 (1977).
5. E. A. Weilmuenster and C. N. Jordan, *J. Am. Chem. Soc.*, **67**, 415 (1945).
6. G. Kallinich, *Arch. Pharm.*, **294**, 90 (1961). The yield of **5a** is increased to 90% by the drop-wise addition of an aqueous solution of acetaldehyde to the alkaline solution of 5-methyl-2-furaldehyde (equimolar amount) at 0°.
7. A. C. Cope and E. R. Trumbull, *Organic Reactions*, **11**, 317 (1960).
8. Conventional glassware was used. The reaction flask was warmed with a heat gun; once initiated, elimination proceeds without further application of heat and is complete (10 mmol scale) in about a minute. Pyrolysate vapors were passed through three cold traps at, in order, -2, -25, and -78°. Product **6** is retained in the first trap.
9. The crude product mixture deposits crystals of **7** on storage in a freezer.
10. Elemental analyses and the complete spectral data support the assigned structure.
11. We are aware of only one other example where a xylylene-type intermediate dimerizes in a head-to-tail manner: Luhowy and Keehn in Ref. 4.
12. H. Ogawa, M. Kubo, and I. Tabushi, *Tetrahedron Lett.*, 361 (1973); H. Ogawa, I. Tabushi, H. Kato, and Y. Taniguchi, *Tetrahedron Lett.*, 5065 (1973).
13. Subsequent to this work, compound **12** was prepared by a route involving the cross-dimerization of **1** and the vinylog of **2**: P. S. Hammond and D. T. Longone, *Tetrahedron Lett.*, 415 (1978).