

# Synthesis and Reduction of 5,5-Dimethyl-2,4-bis(3,4-dimethoxyphenyl)- 2-chloro-2,5-dihydrofuran

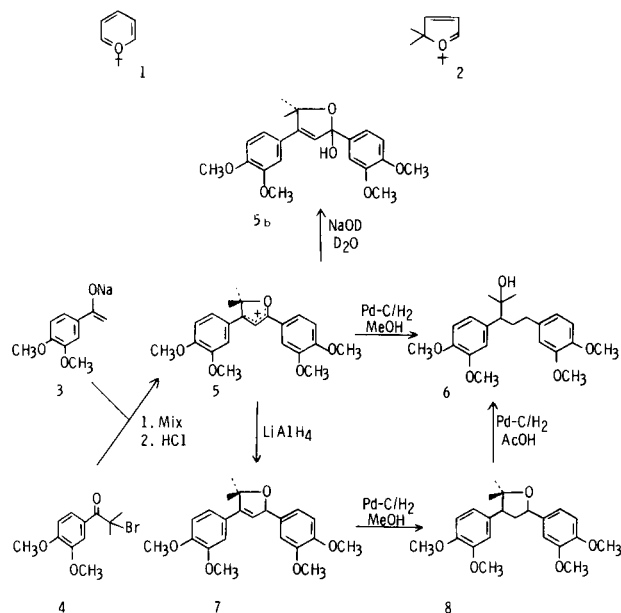
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A new, stable 5-membered ring heterocyclic cation was prepared and reduced into the corresponding dihydrofuran, tetrahydrofuran and pentanol derivatives.

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Pyrylium [1,2] salts **1** are well characterized six-membered ring organic cations which are stable in aqueous solution as long as the pH is kept low [3]. This extra stability was attributed to the fact that the  $\pi$  system of the pyrylium ring has six electrons and thus has aromatic character similar to that of benzene or pyridine. Mesoionic compounds [4,5], five-membered ring heterocycles possessing a sextet of electrons but which cannot be represented satisfactorily by only one covalent or polar structure, are also well-known. However, 5-membered ring non-aromatic stable organic cations, "furylium cations" **2**, have not been studied extensively [6]. In this paper, we would like to report the preparation and characterization of such a salt.



Reaction of the sodium enolate of 3,4-dimethoxyacetophenone **3** with  $\alpha$ -bromo- $\alpha$ -methyl-3,4-dimethoxypropenone **4** gave a light yellow solution which upon treatment with mineral acid gave **5** in good yield. Compound **5** is a red solid which is sparingly soluble in diethyl ether, ethyl acetate and methylene chloride and water. Its solu-

tion in water is orange turning yellow with dilution. Like pyrylium salts, the color disappears when exposed to ammonia vapor, or if dissolved in alkaline solution and reverses back to orange upon acidification. The pmr of **5** gave a single signal ( $\delta$  1.60) for the two geminal dimethyl groups indicating the planar nature of the heterocyclic ring. However upon treatment with sodium deuterium oxide-deuterium oxide, the resulting colorless solution gave two signals for the methyl groups of **5b** ( $\delta$  1.64, 1.76).

The structure of **5** was deduced from the following chemical transformations. Reduction of **5** with Pd-C as a catalyst gave the tertiary alcohol **6** quantitatively. However, reduction of **5** with lithium aluminum hydride gave 5,5-dimethyl-2,4-bis(3,4-dimethoxyphenyl)-2,5-dihydrofuran **7** which was further reduced catalytically to the 3,4-bis(3,4-dimethoxyphenyl)-2,2-dimethyltetrahydrofuran **8**. Hydrogenolysis of **8** in acetic acid gave **6**. These chemical transformations suggest that **5** is a 5-membered ring cation which is stabilized by two 3,4-dimethoxyphenyl substituents. Proton and carbon nmr spectra of **7** and **8** with the proper assignments are given in Figures 1 and 2.

The conversion [7] of primary amines to a wide range of functional groups by using pyrylium cations is well established. The application of the stable furylium cation **5** and other analogous compounds in a similar reaction is the subject of further investigation.

## EXPERIMENTAL

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. Ultraviolet and visible spectra were taken on a Cary 18 spectrophotometer. The nmr spectra were taken on Varian XL-100 or T-60 spectrophotometers, using tetramethylsilane as the internal reference. Mass spectra were obtained on a Finnigan Model 731 spectrophotometer. Elemental analysis were performed by Research and Development Labs. of Merck and Co., Inc., Rahway, New Jersey.

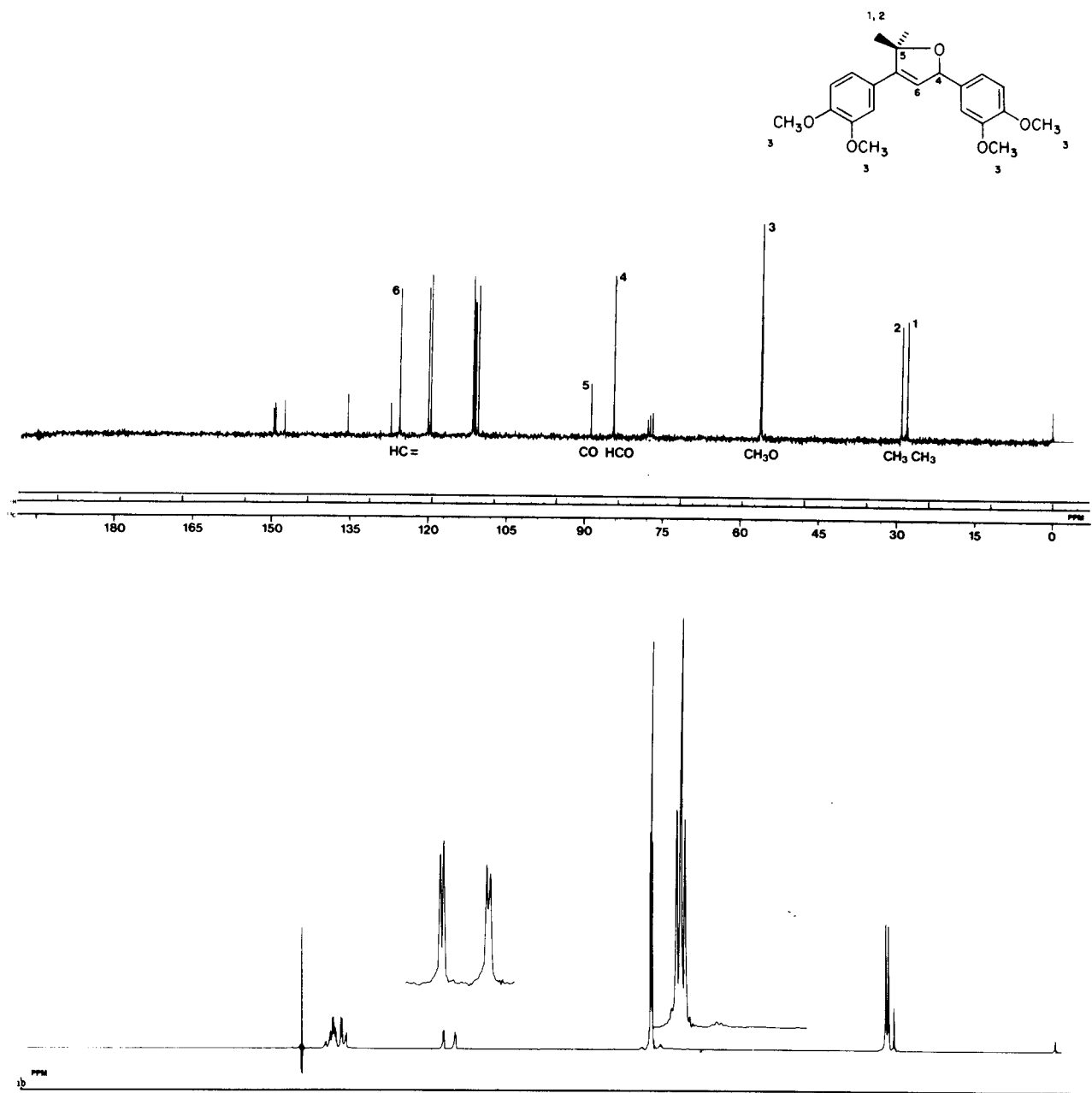
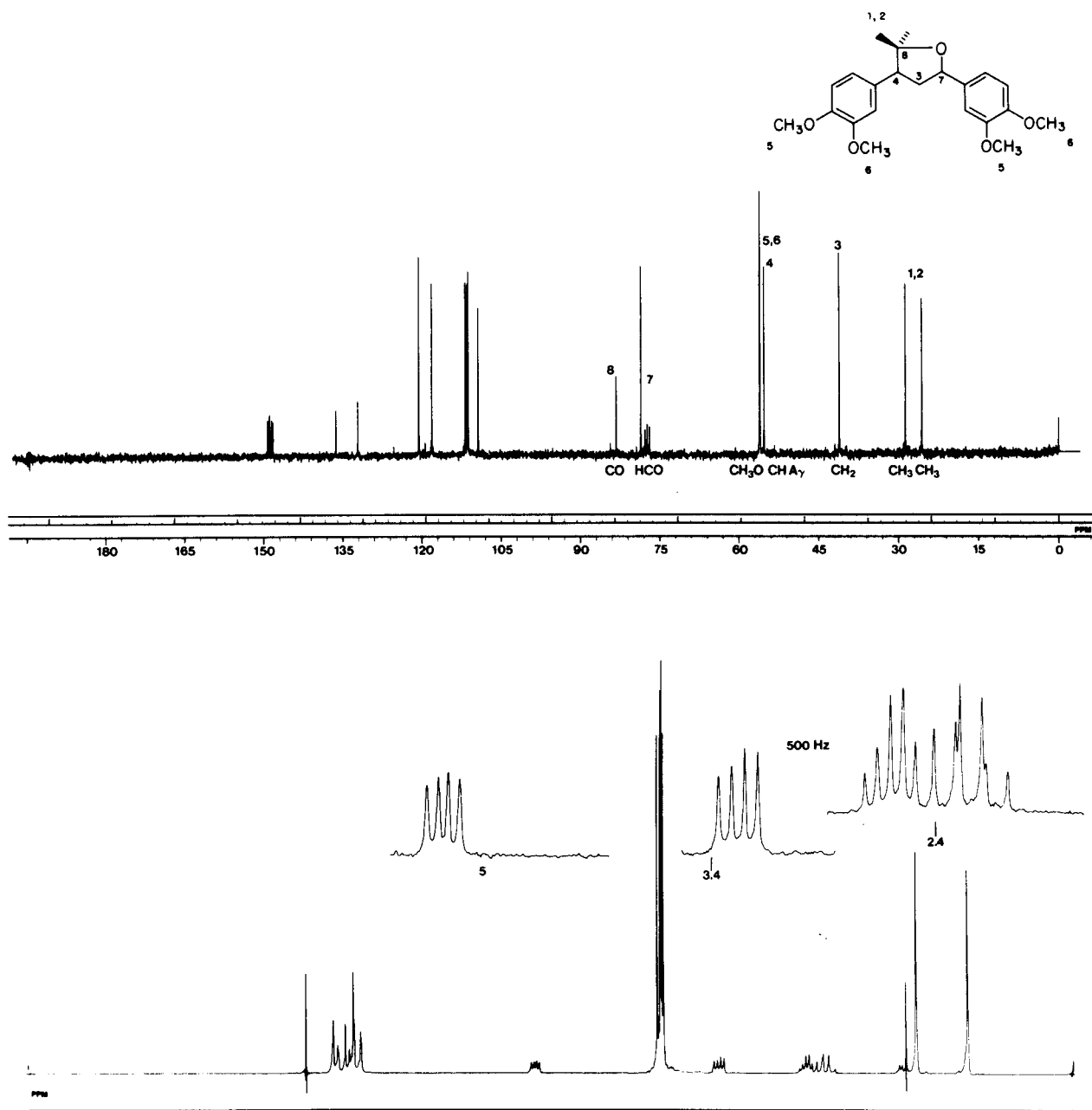


Fig. 1 Decoupled  $^{13}\text{C}$ -NMR (top) and  $^1\text{H}$ -NMR of Dihydrofuran 7

Fig. 2 Decoupled  $^{13}\text{C}$ -NMR and  $^1\text{H}$ -NMR of Tetrahydrofuran **8**

Preparation of 5,5-Dimethyl-2,4-bis(3,4-dimethoxyphenyl)-2-chloro-2,5-dihydrofuran (**5**).

3,4-Dimethoxyacetophenone **3** (7.2 g) in 20 ml of dry tetrahydrofuran was added to a suspension of 0.8 g of sodium hydride in 20 ml of tetrahydrofuran at 0° under nitrogen. After 1 hour of stirring, 4.5 g of  $\alpha$ -bromo- $\alpha$ -methyl-3,4-dimethoxyacetophenone **4** was added and stirred for two days at ambient temperature. The reaction mixture was first treated with 10 ml of distilled water and then 100 ml of ether. The ether layer was washed with water, dried over anhydrous magnesium sulfate (surface of magnesium sulfate turned red), evaporated and redissolved in 50 ml of ethyl acetate. The solution upon treatment with 2 ml of concentrated hydrochloric acid gave red crystalline solid, which was washed several times with ether and air dried to yield 5.5 g of red solid, mp 216-218° (with bubbling); ms: m/e 369 (M<sup>+</sup> - Cl); uv-vis (methanol):  $\lambda$  max 270 (log  $\epsilon$  = 4.03), 485 (log  $\epsilon$  = 4.32).

*Anal.* Calcd. for C<sub>22</sub>H<sub>25</sub>ClO<sub>5</sub>: C, 62.53; H, 6.22. Found: C, 62.40; H, 6.17.

3,5-bis(3,4-Dimethoxyphenyl)-2-methyl-2-pentanol (**6**).

Compound **5** (386 mg) and 10% Pd/C (200 mg) in 50 ml of methanol was stirred over hydrogen at 40 psi for 3 days to yield after usual workup 375 mg of oily product; ms: m/e 374 (M<sup>+</sup>); pmr (deuteriochloroform):  $\delta$  1.16 (6H, s, 2 × CH<sub>3</sub>), 1.6-2.8 (5H, m, CHCH<sub>2</sub>CH<sub>2</sub>), 3.83 and 3.88 (each 6H, s, OCH<sub>3</sub>), 6.5-6.8 (6H, m, Ar-H).

*Anal.* Calcd. for C<sub>22</sub>H<sub>30</sub>O<sub>5</sub>: C, 70.56; H, 8.07; O, 21.36. Found: C, 70.52; H, 8.10; O, 21.41.

5,5-Dimethyl-2,4-bis(3,4-dimethoxyphenyl)-2,5-dihydrofuran (**7**).

Lithium aluminum hydride (150 mg) was suspended in 20 ml of dry tetrahydrofuran and treated with 900 mg of **5** at 0°. After stirring for 30 minutes at 0° and ambient temperature for 2 hours, 2 ml ethyl acetate followed by 3 ml 10% sodium hydroxide added and stirred for 10 minutes. To that, few grams of anhydrous sodium sulfate, 50 ml ether were added and filtered. The residue was washed with 50 ml of ether. The combined ether extract was evaporated to yield colorless oil which was crystallized from ether-hexane to yield 515 mg of prisms, mp 113-114°; pmr (deuteriochloroform):  $\delta$  1.62 and 1.66 (each 3H, s, 2 × CH<sub>3</sub>), 3.92,

3.93 and 3.94 (3H, 6H and 3H respectively, s, -OCH<sub>3</sub>), 5.81 (1H, d, J = 1.8 Hz, 2-H), 5.93 (1H, d, J = 1.3 Hz, 3-H), 6.86-7.08 (6H, m, Ar-H); uv-vis (methanol):  $\lambda$  max 264 (log  $\epsilon$  = 4.13); ms: m/e 370 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>22</sub>H<sub>26</sub>O<sub>5</sub>: C, 71.33; H, 7.07; O, 21.59. Found: C, 71.26; H, 7.11.

5,5-Dimethyl-2,4-bis(3,4-dimethoxyphenyl)tetrahydrofuran (**8**).

Compound **7** (370 mg) and 50 mg of 10% Pd/C in 30 ml of ethyl acetate was stirred over hydrogen at 40 psi for 3 hours and then filtered and evaporated. Crystallization of the residue from methanol gave colorless prisms, mp 138-139°; pmr (deuteriochloroform):  $\delta$  1.00 (3H, s, -CH<sub>3</sub>), 1.49 (3H, s, CH<sub>3</sub>), 2.25-2.60 (2H, m, 3-H), 5.10 (1J, dd, J = 6.0 Hz, 12.5 Hz, 4-H), 3.89, 3.90, 3.92 and 3.95 (each 3H, s, -OCH<sub>3</sub>), 5.10 (1J, dd, J = 6.0 Hz, 10.5 Hz, 2-H), 6.78-7.04 (6H, m, Ar-H); uv-vis (methanol):  $\lambda$  max 229 (log  $\epsilon$  = 3.99), 276 (log  $\epsilon$  = 3.52); ms: m/e 372 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>22</sub>H<sub>28</sub>O<sub>5</sub>: C, 70.94; H, 7.57; O, 21.48. Found: C, 70.90; H, 7.62.

Reduction of **8** (100 mg) in acetic acid (25 ml) with 50 mg 10% Pd-C gave 76 mg of the alcohol **6**.

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