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SYNTHESIS OF 4,5-DIHYDROBENZO[b]FURANS, 4,5-DIHYDROBENZO[b]THIOPHENES, AND 4,5-DIHYDROINDOLES VACUUM PYROLYSIS - ELECTROCYCLIC REACTIONS

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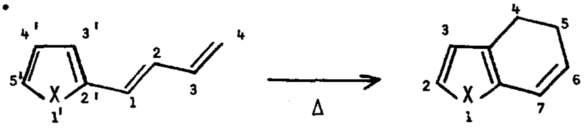
We should like to report the results of the following gas phase vacuum pyrolysis reactions: 1-(2'-furyl)-1,3-butadiene (I)[1] yields 4,5-dihydrobenzo[b]furan (II) 70%; 1-(2'-furyl)-1,3-butadiene-4,4-d_2 (I-d_2) yields 4,5-dihydrobenzo[b]furan-4,4-d_2 (II-d_2) 73%; 1-(2'-thienyl)-1,3-butadiene (III) yields 4,5-dihydrobenzo[b]thiophene (IV) 72%; 1-(2'-N-methylpyrryl)-1,3-butadiene (V) yields 4,5-dihydro-N-methylindole (VI) 90%; and finally 1-(2'-N-methylpyrryl)-1,3-pentadiene (VII) yields 4,5-dihydro-4,N-dimethylindole (VIII) 56% yield. Yields are corrected for recovered starting material (10-30%), which was the only other product observed in these reactions.



X = O, S, N-CH_3

The pyrolysis conditions (particularly pressure) are critical. Thus pyrolysis of I has been reported to yield a mixture of 4,5- and 6,7-dihydrobenzo[b]furans and benzo[b]furan.[2] Likewise, pyrolysis of II has been reported to yield a mixture 4,5- and 6,7-dihydrobenzo[b]-thiophenes and benzo[b]thiophene.[2] The regioselective formation of these 4,5-dihydro isomers is consistent with the three step mechanism previously proposed to account for the formation of 1,2-dihydronaphthalene on pyrolysis of 1-phenyl-1,3-butadiene in the gas phase.[3] For example, in the case of I, the first step is an isomerization of trans-I to cis-I. This step is essential since only the cis isomer has the proper geometry to undergo the second step, a thermally allowed disrotatory electrocyclic reaction converting a conjugated triene composed of the two double bonds of the 1,3-butadiene and 2π electrons from the furan ring into a 1,3-cyclohexadiene.[4-7] This process involves partial disruption of the aromatic 6π electron system of the furan ring. Several examples of participation of 2π electrons from benzene[8,9] and pyridine[10] rings in thermal electrocyclic reactions have been reported. The final step is a 1,5-sigmatropic suprafacial hydrogen migration leading to restoration of the furan nucleus.[11]

4,5-Dihydrobenzo[b]furan, 4,5-dihydrobenzo[b]thiophene, and 4,5-dihydroindole are unknown ring systems. The simplicity and generality of this approach to the preparation of these 4,5-dihydro ring systems can be contrasted to the variety of methods used to prepare the known dihydrobenzo[b]furan, dihydrobenzo[b]thiophene, and dihydroindole isomers. Two isomers of dihydrobenzo[b]furan are known: 3,4-dihydrobenzo[b]furan is quite common; the other, 3a,7a-dihydrobenzo-[b]furan, is formed on photolysis of oxinin.[12-14] Likewise, two isomers of dihydrobenzo[b]-thiophene have been reported. 3,4-Dihydrobenzo[b]thiophene has been known for fifty years.[15-17] An attempt to prepare IV has been reported. Reduction of 4,5,6,7-tetrahydro-7-keto-thiophene led to the corresponding alcohol. However, attempted dehydration with PPA gave polymer, leading to the conclusion that IV was unstable.[18] Three isomers of dihydroindole have been prepared. 2,3-Dihydroindole is well known. Hydrogenation of indole over PtO_2 in a mixed $EtOH/HBF_4$ solvent provides an efficient route to 2,3-dihydroindoles.[19] Birch reduction of indole with Li in liq. NH_3 in the presence of CH_3OH yields 4,7-dihydroindole.[20,21] Finally, isomerization of the initial product from the Wittig reaction of methylenetriphenylphosphorane with 4,5,6,7-tetrahydro-4-keto-indole led to 6,7-dihydro-4-methylindole.[22]

The starting 1,3-butadienes (I, I-d_2, III, V, and VII) were easily prepared by Wittig reactions. I, III, and V were prepared by reaction of allylenetriphenylphosphorane with furfural 30%, with 2-thiophenecarboxaldehyde 28%, and with N-methylpyrrole-2-carboxaldehyde 31% yield respectively. I-d_2 was prepared by reaction of 2-(2'-furyl)-propenal with the Wittig reagent prepared from methyl-d_3-triphenylphosphonium iodide in 54% yield.[23] VII was prepared by reaction of M-methylpyrrole-2-carboxaldehyde with the Wittig reagent prepared from crotyltriphenylphosphonium bromide in 80% yield. Samples of I, I-d_2, and III were purified by prep. GLC on a 1/4" x 10', 20% polyphenyl ether (6 ring) on Chromosorb P column at 170° (GLC-A). Their properties were in agreement with literature values.[1] The nmr of I-d_2 had the expected changes. Samples of V and VII were purified by prep. GLC on a 1/4" x 6', 20% FFAP (varian) on Chromosorb P, which had been modified by the addiiton of 10% powdered KOH, column at 170° (GLC-B). V and VII were characterized by nmr, ir, and uv. The products II, II-d_2, and IV were purified by prep. GLC-A. The products VI and VIII were purified by prep. GLC-B. The products were characterized by nmr (See Table I), uv (See Table II), ir, and mass spectrometry. Satisfactory elemental analysis was obtained for IV.[24] The elemental composition of the parent ions of II, VI, and VIII were determined by peak matching using high resolution mass spectrometry.[25] In addition, IV was dehydrogenated by treatment with DDQ in refluxing DME to yield benzo[b]thiophene.[26]

Pyrolysis Apparatus and Conditions. The pyrolyses were performed using a 30 cm vertical tube oven. The diameter of the heated zone was 3.5 cm. The pyrolysis tube was made from quartz (9 mm O.D., 8 mm I.D.), 250 cm long. It was wrapped in the form of a helical spiral of 30 turns, 30 cm in height. A 10 ml round bottom flask containing a Teflon covered magnetic stirring bar and 5-6 mmol of I, I-d_2, III, V, or VII to be pyrolyzed was connected to the bottom of the pyrolysis tube. The top of the pyrolysis tube was attached to a cold finger condenser cooled with liquid N_2. The outlet of the condenser was connected to a vacuum pump. The pyrolysis tube was heated (525 - 575°C). The samples of I, I-d_2, III, V, or VII were distilled under vacuum (1.0 to 0.1 mm) into the pyrolysis tube by warming the round bottom flask. Under these conditions, 5-6 mmol of sample passed through the pyrolysis tube in 15-30 min. Thus the contact time is ≈0.1 sec. After completion of the pyrolysis, the cold finger condenser, with the pyrolysate frozen onto it, is disconnected from the pyrolysis tube and connected to a 10 ml round bottom flask. After the coolant evaporates, the product drips off the condenser into the flask.

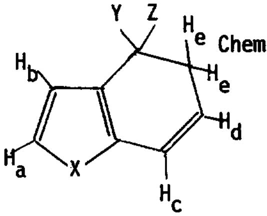


Table I - NMR Spectra

Chemical Shifts δ, Coupling Constants Hz

II X = O, Y = Z = H

II-d_2 X = O, Y = Z = D

IV X = S, Y = Z = H

VI X = N-CH_3, Y = Z = H

VIII X = N-CH_3, Y = H, Z = CH_3

Compound	X	H_a	H_b	H_c	H_d	H_e	Y	Z
II		7.20 (d,J=2)	6.20 (d,J=2)	6.34 (d,J=10)	5.72 (txd,J=10,4)	2.36 (m)	2.60 (m)	
II-d_2		7.20 (d,J=2)	6.24 (d,J=2)	6.34 (d,J=10)	5.84-5.66 (br. m)	2.36 (br. s)		
IV		7.08 (d,J=6)	6.82 (d,J=6)	6.48 (d,J=10)	5.84 (txd,J=10,5)	2.36 (m)	2.80 (t,J=8)	
VI	3.62 (s)	6.44 (d,J=4)	5.94 (d,J=4)	6.34 (d,J=10)	5.72 (txd,J=10,4)	2.44 (m)	2.74 (t,J=8)	
VIII	3.62 (s)	6.46 (d,J=3)	6.00 (d,J=3)	6.36 (d,J=10)	5.72 (txd,J=10,4)	2.6-1.9 (br. m)	2.98 (m)	1.36 (d,J=7)

Spectra were recorded on a Varian XL-100

Table II - Ultraviolet Spectra.

λ_{max} in Å, ($\varepsilon \times 10^{-3}$).

Compound					
II	3040 (3.58);	2900 (7.40);	2810 (7.89)		
IV	3080 (3.26);	2940 (8.15);	2840 (8.42);	2310 (4.13);	2220 (5.43)
VI	3160 (1.31);	3020 (2.50);	2900 (2.96);		2200 (3.92)
VIII	3160 (5.15);	3006 (8.48);			2230 (9.15)

All Spectra were taken in spectro-quality cyclohexane on a Beckman Acta M Spectrometer.

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