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SYNTHESIS AND TAUTOMERIC STUDIES OF 1-BENZYLISOBENZOFURAN AND RELATED COMPOUNDS

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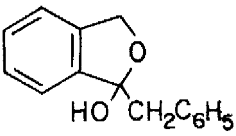
Recently, Smith and Wikman[1] reported that 1-benzyl-1-hydroxyphthalan (1) undergoes intramolecular loss of water to afford 1-benzalphthalan (2c). Although the tautomer, 1-benzylisobenzofuran (6c) could not be isolated, its presence in solution was inferred by formation of Diels-Alder adduct 3 with dimethyl acetylenedicarboxylate. These investigators, using uv and nmr spectroscopy, were unable to observe directly the existence of an equilibrium between 2c and isomer 6c. Experience gained from the preparation of isoindole[2a] and its derivatives[2b] by retro-Diels-Alder reaction effected by flash vacuum thermolysis suggested to us that the elusive 1-benzylisobenzofuran (6c) might be amenable to synthesis and isolation by application of this technique to the 1,4-epoxynaphthalene 5c[3]. We now report that flash thermolysis of 5c not only affords 6c, but is also a practical method for the preparation of 1-methylisobenzofuran (6a) and 1,3-dimethylisobenzofuran (6b). In addition, we describe the results of spectral studies of these heterocycles (6a-c) which corroborate the claim of Smith and Wikman[1a] of the existence of a tautomeric equilibrium between 2c and 6c.



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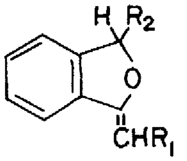

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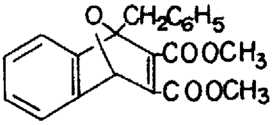

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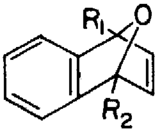
a. R_1=H; R_2=H
b. R_1=H; R_2=CH_3
c. R_1=C_6H_5; R_2=H

Reaction of 2-benzylfuran[4] with benzyne [5a] gave adduct 4c (Table I). In similar fashion, treatment of 2-methylfuran and 2,5-dimethylfuran with benzyne gave the known 1,4-dihydro-1,4-epoxynaphthalenes 4a (56%) and 4b (50%), respectively.[5] Hydrogenation of adducts 4a-c in 95%

ethanol with 10% palladium-charcoal (40 psi, 20°) for 45 min produced the corresponding 1,2,3,4-tetrahydro-1,4-epoxynaphthalenes 5a-c (Table I). Flash thermolysis of 5a-c at 600° (0.5mm) by the usual method[2] gave ethylene and essentially quantitative yields of the corresponding isobenzofurans 6a-c as white crystals which were collected in a trap cooled by liquid nitrogen. These products were extremely reactive at room temperature and resinified rapidly. Compounds 6a-c were characterized by their spectral properties (Table II) and by formation of Diels-Alder adducts. Thus, with dimethyl acetylenedicarboxylate 1-benzylisobenzofuran (6c) gave 3[1a]. Both 1-methylisobenzofuran (6a) and 1,3-dimethylisobenzofuran (6b) with N-phenylmaleimide in ether gave mixtures of their respective *exo*- and *endo*-adducts 7 which were resolved with partial success by fractional crystallization from chloroform-hexane. Whereas *exo*- and *endo*-adducts 7a were obtained analytically pure, only *endo*-adduct 7b was isolated in the pure state (Table I).



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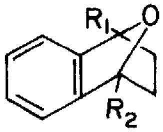

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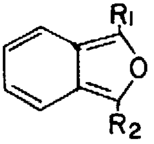

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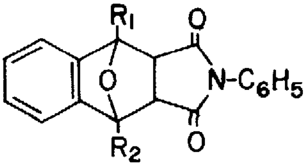

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a, R_1=CH_3, R_2=H; b, R_1=R_2=CH_3; c, R_1=$CH_2C_6H_5$, R_2=H

The time-evolution of the nmr spectrum of 1-benzylisobenzofuran (6c) in $CDCl_3$ at room temperature is shown in the accompanying figure. The signals in Spectrum A are attributable solely to 6c (Table II). Spectrum C, in contrast, is identical to that of 1-benzalphthalan (2c).[1b] The intermediate Spectrum B shows disappearing signals of 6c and emerging signals of 2c. Equilibrium in this case was established in about 4 hr, whereas with C_6D_6 as solvent up to 20 hr was required. Addition of a trace of trifluoroacetic acid to 6c in either solvent effected equilibration almost instantaneously. Interestingly, the equilibration was promptly arrested by addition of one drop of triethylamine.

Similar spectral studies conducted in $CDCl_3$ on 1-methylisobenzofuran (6a) and 1,3-dimethylisobenzofuran (6b) failed to reveal the existence of a tautomeric equilibrium between them and their corresponding 1-methylenephthalan isomers 2a and 2b. No evidence could be found for the presence of the latter under the conditions used in this study. Unlike 6c, isobenzofurans 6a and 6b decomposed rather quickly in solution at room temperature; the presence of triethylamine retarded this decomposition somewhat. Compounds 6a and 6b were instantly destroyed in solution on addition of a trace of trifluoroacetic acid.

Table I

Properties of Intermediates and Diels-Alder Adducts

Compd[6]	Appearance	Yd,%	Mp,°C	Bp,°C(mm)	Nmr ($CDCl_3$),δ,[ir (C=O),cm^{-1}]
4c	Pale orange needles	64	98.8-99.5	-	3.55(d,2),5.55(d,1),6.64-7.42(m,11)
5a	Pale yellow liq.	95	-	95-97(7.0)	1.76(s,3),1.21-2.29(m,4),5.2(d,1),6.96-8.24 (m,4)
5b	Colorless liq.	61	-	44-45(0.2)	1.77(s,3),1.19-2.0(m,4),6.97-7.12(broad s,4)
5c	Wt. crystals	90	75.2-75.9	-	1.14-2.19(m,4),3.46(d,2),5.23(d,1),6.97-7.39(m,4)
7a (exo)	Wt.crystals	18	201-201.6	-	1.88(s,3),2.95(q,2),5.62 (s,2),6.9-7.58(m,4),[1730]
7a (endo)	Light yellow plates	14	153-153.5	-	1.94(s,3),3.38(d,1),3.79-4.30(q,1),5.6(d,1),6.14-6.43 (m,2),6.99-7.33(m,7),[1730]
7b (endo)	Wt. crystals	60[7]	215-217	-	2.07(s,3),3.49(s,2),5.96-6.17(m,2),6.84-7.51(m,7),[1720]

Table II

Spectral Properties of Isobenzofurans

Compd	UV(Heptane),nm.	Nmr ($CDCl_3$),δ
6a	357,347,340,332,324,317,309,291,282,270,251,244,236,207,(λmax)	2.56(s,3),6.59-6.81(m,2),7.06-7.21(m,2),7.74(s,1)
6b	375,366,356,347,339,331,325,308,244,216 (λmax)	2.48(s,6),6.46-6.68(m,2),6.93-7.21(m,2)
6c	357,347,339,332,323,317,293,281,271,250,208 (λmax)	4.27(s,2),6.58-6.89(m,2),7.02-7.53(m,7),7.81(s,1).

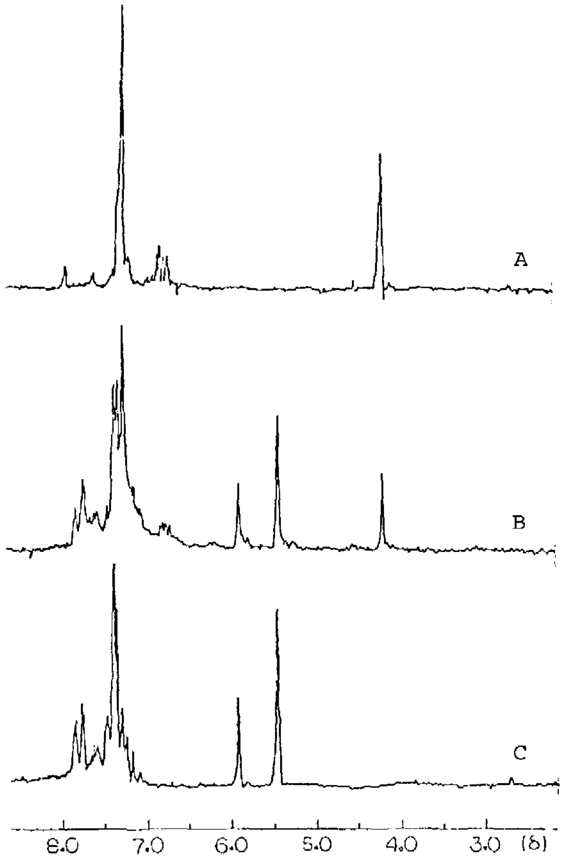

Figure. Time-Dependency of NMR Spectra of 6c in $CDCl_3$ at Room Temperature

A. Immediately after Dissolution

B. After 1 Hr.

C. After 4 Hr.

In addition to confirming that benzenoid structure 2c is more stable than its o-quinonoidal tautomer 6c, the foregoing observations indicate that the phenyl substituent plays an important role in the tautomeric equilibrium between these compounds. It is conceivable that the apparently greater stability of phthalan 2c relative to the phthalans 2a and 2b results from a combination of extended conjugation involving the phenyl group and resonance interaction between this group and the oxygen atom.

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References and Notes

(1) (a) J.G. Smith and R.T. Wikman, J. Org.Chem., 39, 3648 (1974).
    (b) J.G. Smith and R.T. Wikman, Tetrahedron, 30, 2603 (1974).
(2) (a) J. Bornstein, D.E. Remy, and J.E. Shields, Chem. Commun., 1149 (1972).
    (b) J. Bornstein, D.E. Remy, and J.E. Shields, Tetrahedron Lett., 4247 (1974).
(3) U.E. Wiersum and W.J. Mijs [Chem..Commun., 347 (1972)] used this technique for the preparation of the parent isobenzofuran.
(4) R. Paul, C.R. Acad.Sci., 200, 1481 (1935).
(5) (a) L.F. Fieser and M.J. Haddadin, Can. J. Chem., 43, 1599 (1965).
    (b) E. Walthuis, J. Org. Chem., 26, 2215 (1961).
(6) Satisfactory elemental analyses were obtained for these compounds.
(7) This value includes both the exo- and endo-adducts.