

A Novel Isobenzofuran Derivative Undergoing Photovalence Isomerization

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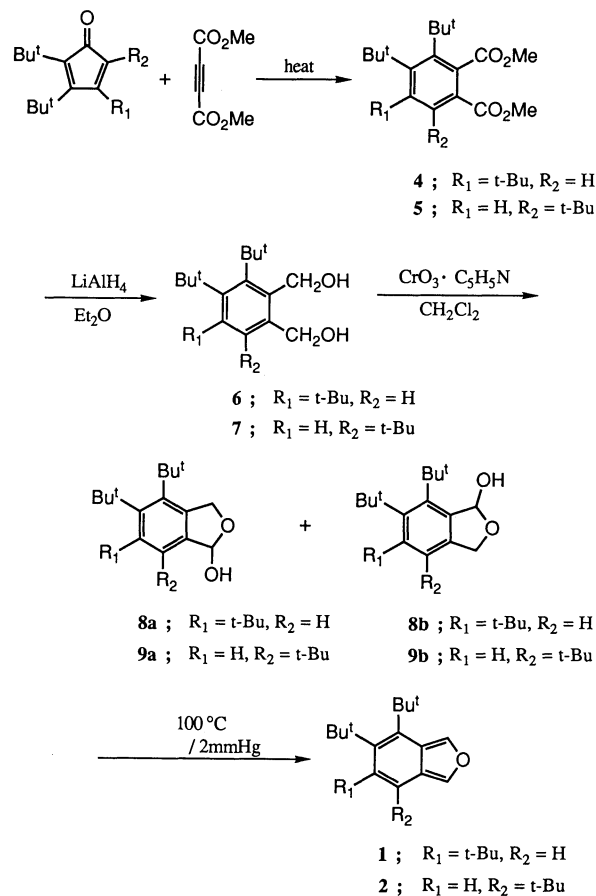
Synopsis. 4,5,6-Tri-*t*-butylisobenzofuran (**1**) and 4,5,7-tri-*t*-butylisobenzofuran have been synthesized. They were stable infinitely in solutions at room temperature. Upon irradiation, **1** undergoes photovalence isomerization to afford 2,3,4-tri-*t*-butyl-8-oxatetracyclo [4.3.0.0^{2,4}.0^{3,5}]nona-1(9),6-diene.

Isobenzofuran and its derivatives have been widely studied in view of their aromaticity¹⁾ as well as their potential as a synthon in organic synthesis.²⁾ We have been interested in this molecule in the context of our study on photochemical reactivity of overcrowded polycyclic aromatic compounds. Previously, we reported³⁾ that 4,5,7-tri-*t*-butylisobenzofuran (**2**) was a *stable but electronically undisturbed* derivative suitable for studying inherent reaction behavior of the skeleton. In this paper we wish to report a new isobenzofuran derivative, 4,5,6-tri-*t*-butylisobenzofuran (**1**), which underwent photovalence isomerization to 2,3,4-tri-*t*-butyl-8-oxatetracyclo [4.3.0.0^{2,4}.0^{3,5}]nona-1(9),6-diene, together with synthetic details for **1** and **2**.

Results and Discussion

4,5,6-Tri-*t*-butylisobenzofuran (**1**) was synthesized according to the method outlined in Scheme 1. Oxidation of 3,4,5-tri-*t*-butyl-1,2-benzenedimethanol (**6**) with chromic anhydride–pyridine complex afforded 4,5,6-tri-*t*-butyl-1,3-dihydro-1-isobenzofuranol (**8a**) and 5,6,7-tri-*t*-butyl-1,3-dihydro-1-isobenzofuranol (**8b**) with recovery of **6**. Increasing the amount of the oxidizing agent decreased the recovery of **6**. However, this did not lead to the increase of the yield of **8** because of the formation of further oxidized products. A condition optimized for getting **8** is reported in Experimental part. Dehydration of **8** proceeded to give **1** by heating **8** under reduced pressure. 4,5,7-Tri-*t*-butylisobenzofuran (**2**) was obtainable by a similar method starting from 3,4,6-tri-*t*-butyl-1,2-benzenedimethanol (**7**).

Isobenzofurans, **1** and **2**, were stable even in solution, and under anaerobic conditions no detectable change was observed by NMR analysis after standing for a month at ambient temperature. Isobenzofuran derivatives tractable at ambient conditions known so far possess π conjugative substituents, and they are stable by virtue of π delocalization. On the other hand, being devoid of π conjugative substituents, change of **1** and **2** in electronic structure from the parent molecule seems to be small. In fact, the electronic spectra of **1** and **2** (Figure 1) are very similar to that of the parent molecule⁴⁾ except for lacking of vibrational progressions, which was observed in the case of the parent molecule, indicating that **1** and **2** are electronically undisturbed system. The longest absorption band for **1** appeared at somewhat



Scheme 1.

shorter wavelength region in comparison with that for **2**. This is probably due to reduced coplanarity of the π structure of **1** by the out-of-plane bending deformation of the molecular skeleton caused by the repulsive non-bonded interaction between the *t*-butyl groups. The remarkable stabilities of **1** and **2** should be due to the steric substituent effect of the *t*-butyl groups which hinders the molecules from coming into contact with other reactive materials.

Of special interest is a quite unique photochemical feature of **1**. Irradiation of **1** in acetonitrile resulted in the formation of 2,3,4-tri-*t*-butyl-8-oxatetracyclo [4.3.0.0^{2,4}.0^{3,5}]nona-1(9),6-diene (**3**) (Scheme 2), whereas **2** gave benzocyclopropenecarbaldehyde³⁾ via usual photochemical rearrangement of furan to cyclopropene-3-carbaldehyde.⁵⁾ The photoreaction of **1** proceeded with quantum efficiency of 0.02, and **3** was a sole product detectable by NMR analysis.

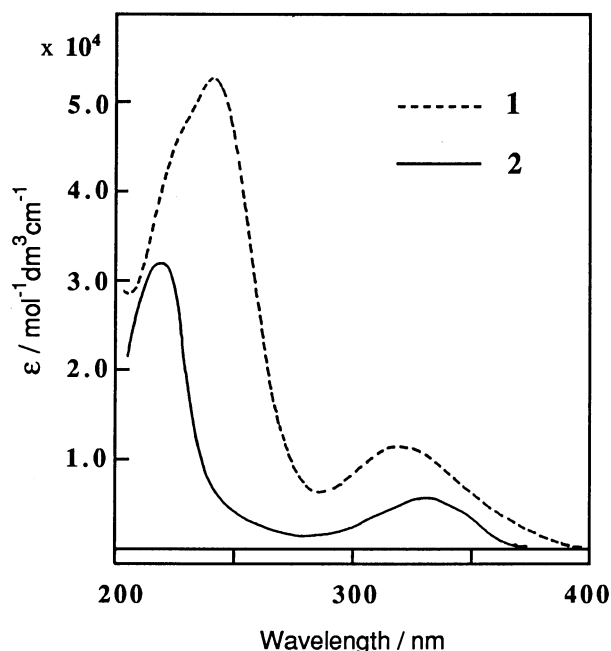
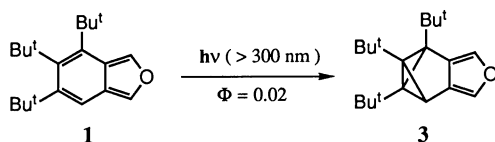


Fig. 1. Electronic spectra of 1 and 2 in acetonitrile.



Scheme 2.

In summary, stable but simple alkyl-substituted derivatives of isobenzofuran were synthesized. The present case is the first example of an isobenzofuran derivative which undergoes phtovalence isomerization.

Experimental

Dimethyl 3,4,5-Tri-*t*-butylphthalate (4). A mixture of 1 g (4 mmol) of 2,3,4-tri-*t*-butyl-2,4-cyclopentadien-1-one⁶ and 1 g (7 mmol) of dimethyl acetylenedicarboxylate was heated at 80°C for 1.5 h. The excess reagent was removed under reduced pressure and the residual materials were chromatographed on silica gel with dichloromethane. Recrystallization from methanol gave white crystals of 4 (1.0 g, 70%); Mp 58°C; ¹H NMR (CDCl₃) δ=7.68 (1H, s), 3.86 (3H, s), 3.81 (3H, s), 1.42 (9H, s), 1.37 (9H, s), and 1.36 (9H, s); IR (KBr) 1722, 1738, and 1270 cm⁻¹; Found: C, 72.63; H, 9.65%. Calcd for C₂₂H₃₄O₄: C, 72.89; H, 9.45%.

Dimethyl 3,4,6-Tri-*t*-butylphthalate (5) was obtained in a similar manner to the synthesis of 4 starting from 2,3,5-tri-*t*-butyl-2,4-cyclopentadien-1-one^{6,7} in the yield of 85%. 5: White crystals; mp 124°C; ¹H NMR (CDCl₃) δ=7.63 (1H, s), 3.80 (3H, s), 3.79 (3H, s), 1.51 (9H, s), 1.46 (9H, s), and 1.35 (9H, s); IR (KBr) 1742, 1730, 1305, 1255, and 1204 cm⁻¹; Found: C, 72.66; H, 9.66%. Calcd for C₂₂H₃₄O₄: C, 72.89; H, 9.45%.

3,4,5-Tri-*t*-butyl-1,2-benzenedimethanol (6). A suspension of lithium aluminum hydride (0.5 g, 13 mmol) in 40 ml anhydrous ether was added a solution of 4 (1.0 g, 2.76 mmol) in the same solvent dropwise under stirring at room temperature. After 1 h the reaction mixture was poured onto water and

extracted with ether. Chromatography on silica gel with hexane-ethyl acetate (1:1) followed by recrystallization from hexane gave white crystals of 6 (0.68 g, 80%); Mp 138°C; ¹H NMR (CDCl₃) δ=6.99 (1H, s), 5.01 (2H, ABq, *J*=12.5 Hz), 4.66 (2H, ABq, *J*=12.2 Hz), 2.75 (2H, br.s), 1.46 (9H, s), 1.40 (9H, s), and 1.36 (9H, s); IR (KBr) 3355, 1479, 1005, and 983 cm⁻¹; Found: C, 78.10; H, 11.37%. Calcd for C₂₀H₃₄O₂: C, 78.38; H, 11.18%.

3,4,6-Tri-*t*-butyl-1,2-benzenedimethanol (7) was obtained from 5 in a similar manner to the synthesis of 6 in the yield of 85%. 7: White crystals; mp 144°C; ¹H NMR (CDCl₃) δ=7.42 (1H, s), 4.99 (2H, s), 4.93 (2H, s), 1.50 (9H, s), and 1.44 (18H, s); IR (KBr) 3360, 3020, 1570, 1420, 1220, and 1140 cm⁻¹; Found: C, 78.15; H, 11.36%. Calcd for C₂₀H₃₄O₂: C, 78.38; H, 11.18%.

4,5,6- and 5,6,7-Tri-*t*-butyl-1,3-dihydro-1-isobenzofuranols (8). A solution of 6 (0.68 g, 2.2 mmol) in 10 ml of dry dichloromethane was added 2.4 mmol of chromium trioxide pyridine complex⁸ in the same solvent at room temperature, and the mixture was stirred for 1 h. The reaction mixture was concentrated to ca. 3 ml and was chromatographed on silica gel with hexane/ethyl acetate (5:2) to give a mixture of 8a and 8b as viscous material in 26% combined yield. Diol 6 of 52% was recovered. Attempts to separate 8a and 8b and to purify them to an analytical grade were unsuccessful, and the mixture of 8a,b thus obtained was used for next step without further purification. ¹H NMR (CD₃CN) of the mixture revealed the two sets of signals with the intensity ratios corresponding to 8a/8b=3/2. 8a: δ=7.14 (1H, s), 6.16 (1H, pseudo triplet, -O-CH-O-), 5.47-5.06 (2H, m, -CH₂-O-); 10 8b: δ=7.06 (1H, s), 6.63 (1H, d, *J*=7.8 Hz, -O-CH-O-), 4.86 (2H, ABq, *J*=12.5 Hz, -CH₂-O-). The *t*-butyl protons of 8a and 8b gave a broad coalescing signal at 1.45-1.37 ppm with three maxima at 1.43, 1.46, and 1.37 ppm.

4,5,6-Tri-*t*-butylisobenzofuran (1). A solution of 8a,b (136 mg, 0.44 mmol) in ether of as small volume as possible was charged into a one-side glass tube with inner diameter of 5 mm and length of 30 cm. The solvent was removed carefully by nitrogen flow. The part of the tube where 8 was pasted on its inner wall was heated at 100°C at 2 mmHg (1 mmHg=133.322 Pa). During heating, the part of glass tube at 10 cm distance from its top was cooled with dry ice. By this method 100 mg (80%) of 1 was collected at the part cooled. The product was pure enough and any impurity was not detected by NMR. Attempts to solidify 1 by recrystallization from various solvents were unsuccessful. 1: Colorless viscous material; ¹H NMR (CD₃CN) δ=7.87 (1H, dd, *J*=1.5 Hz, *J*=0.7 Hz), 7.68 (1H, d, *J*=1.5 Hz), 6.96 (1H, d, *J*=0.7 Hz), 1.55 (s, 9H), 1.37 (s, 9H), and 1.34 (s, 9H); IR (neat) 1493, 1395, 1365, 1205 and 1055 cm⁻¹; HRMS Found: *m/z* 286.22905. Calcd for C₂₀H₃₀O: M, 286.2296.

4,5,7-Tri-*t*-butylisobenzofuran (2). Oxidation of diol (7) with chromium trioxide pyridine complex by the same method to the synthesis of 8 gave a 1:1 mixture of 9a,b in the 27% combined yield. Attempt to separate them fell in vain. ¹H NMR (CDCl₃) of the mixture was composed of two set of signals for 9a,b; δ=7.50 (1H, s), 7.46 (1H, s), 6.86 (1H, d, *J*=8.1 Hz), 6.51 (1H, d, *J*=6.3 Hz), 5.18 (2H, ABq, *J*=11.6 Hz), 5.07 (2H, ABq, *J*=11.6 Hz), 2.51 (1H, d, *J*=6.2 Hz), 2.38 (1H, d, *J*=8.2 Hz), 1.52 (9H, s), 1.46 (9H, s), 1.45 (9H, s), 1.44 (18H, s), and 1.35 (9H, s). The NMR signals could not be divided into the two sets for 9a and 9b, because the composition 9a/9b was very close to unity. The mixture was subjected to dehydration without separation. Thermal dehydration of 9a,b by the method employed for the synthesis of 1 gave 2 in 75% yield. Recrystallization from methanol gave 2 as white crystals: Mp 58-59°C; ¹H NMR (CD₃CN) δ=8.13 (1H, d, *J*=1.8 Hz), 8.05 (1H, d, *J*=1.8 Hz), 6.88 (1H, s), 1.60 (9H, s), 1.46 (9H, s), and 1.38 (9H, s); IR (KBr) 1595, 1075, 885, 845, and 740 cm⁻¹;

HRMS Found: m/z 286.2304. Calcd for $C_{20}H_{30}O$: M, 286.2296; Found: C, 84.13; H, 10.49; O, 5.60%. Calcd for $C_{20}H_{30}O$: C, 83.85; H, 10.56; O, 5.59%.

Photochemical Reaction of 4,5,6-Tri-*t*-butylisobenzofuran (1). A solution of 5 mg of **1** in 0.5 ml of CD_3CN was placed in an NMR sample tube, degassed by freeze and thaw cycles and sealed. The solution was irradiated with a high-pressure Hg-lamp through a K_2CrO_4 solution filter. The reaction was followed by 1H NMR which revealed that **3** was a sole product detectable. Quantum yield for the isomerization was determined by measuring the decrease of the absorption for **1** upon irradiation on a degassed solution of **1** in acetonitrile (2×10^{-4} mol dm^{-3} , 4 ml) at 313 nm. For getting analytical sample, a solution of 50 mg of **1** in acetonitrile was degassed by freeze and thaw cycles and irradiated with a high-pressure Hg-lamp through a K_2CrO_4 solution filter until all of **1** disappeared. Removal of the solvent followed by distillation by using a Kugel-Rohr glass tube afforded **3** (43 mg, 86%) as colorless viscous oil: 1H NMR (CD_3CN) δ =6.79 (2H, br. s), 6.73 (1H, s), 2.18 (1H, s), 1.29 (9H, s), and 1.21 (18H, s); IR (neat) 1475, 1395, 1365, 1005, and 925 cm^{-1} ; HRMS Found: m/z 286.22895. Calcd for $C_{20}H_{30}O$: M, 286.2296.

References

- 1) R. N. Warrener, *J. Am. Chem. Soc.*, **93**, 2346 (1972); D. Wege, *Tetrahedron Lett.*, **1971**, 2337; U. E. Wiersum and W. J. Mijs, *J. Chem. Soc., Chem. Commun.*, **1972**, 347; M. J. S. Dewar, A. J. Harget, N. Trinajstić, and S. D. Worley, *Tetrahedron*, **26**, 4505 (1970); M. H. Palmer and S. M. F. Kennedy, *J. Chem. Soc., Perkin Trans. 2*, **1976**, 81.
- 2) W. Friedrichen, *Adv. Heterocycl. Chem.*, **26**, 135 (1980); U. E. Wiersum, *Aldrichimica Acta*, **14**, 53 (1981).
- 3) S. Miki, M. Yoshida, and Z. Yoshida, *Tetrahedron Lett.*, **30**, 103 (1989).
- 4) R. N. Warener, I. G. Pitt, and R. A. Russell, *J. Chem. Soc. C*, **1982**, 1195.
- 5) R. Srinivasan, *J. Am. Chem. Soc.*, **89**, 4812 (1967); H. Hiraoka, *Tetrahedron*, **29**, 2955 (1973); W. A. Rendall, M. Torres, and O. P. Strausz, *J. Org. Chem.*, **50**, 3034 (1985).
- 6) G. Maier, S. Pfriem, U. Schafer, K. D. Malsch, and R. Matusch, *Chem. Ber.*, **114**, 3964 (1981).
- 7) W. H. Starnes, Jr., D. A. Plank, and J. C. Floyd, *J. Org. Chem.*, **40**, 1124 (1975).
- 8) R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1970).
- 9) The hydroxymethyl protons of **6** gave the NMR signals of AB-quartet probably due to the formation of a non-planar ring through hydrogen bond. This was not observed in case of **7**.
- 10) The methylene and methyne protons of **8a** gave complicated multiplet signals. This is due to the existence of two types of out-of-plane ring deformation of the phenyl ring, that is, in one type the *t*-butyl groups at C4 and C6 positions are in the same direction to the hydroxyl group, and in the other, the *t*-butyl groups are in the opposite direction to the hydroxyl group. This is not the case for **8b**, because the hydroxyl group and the adjacent *t*-butyl group should avoid eclipsing conformation in the case of **8b**. Therefore, **8b** exists in one isomer with respect to the out-of-plane bending deformation of the phenyl ring.