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A Novel Isobenzofuran Derivative Undergoing Photovalence Isomerization

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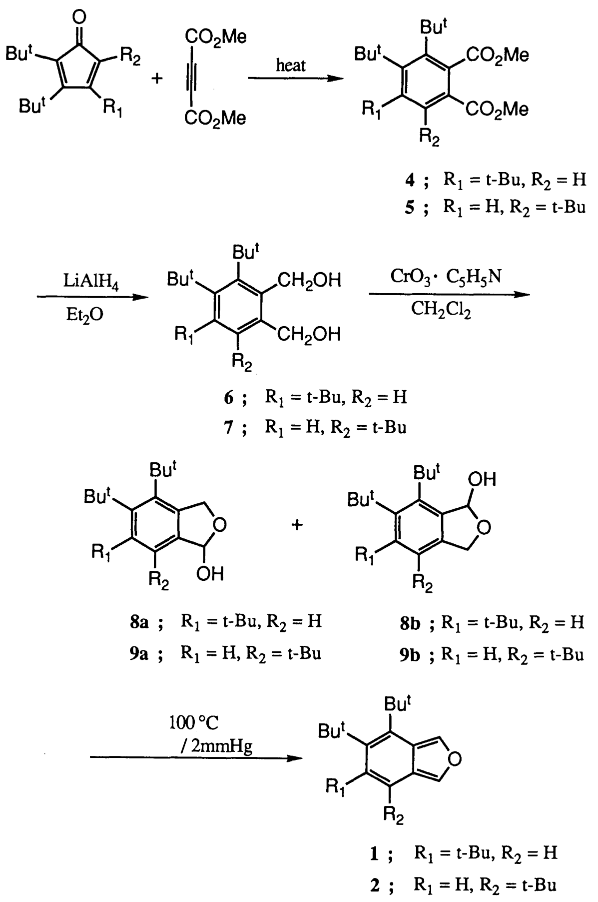
Synopsis. 4,5,6-Tri-*t*-butylisobenzofuran (**1**) and 4,5,7-tri-*t*-butylisobenzofuran have been synthesized. They were stable infinitely in solutions at room temperature. Upon irradiation, **1** undergoes photovalence isomerization to afford 2,3,4-tri-*t*-butyl-8-oxatetracyclo [4.3.0.$0^{2,4}$.$0^{3,5}$]nona-1(9),6-diene.

Isobenofuran and its derivatives have been widely studied in view of their aromaticity[1] 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 reported[3] 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 molecule[4] 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 shorter wavelength region in comparison with that for **2**. This is probably due to reduced coplanality of the π structure of **1** by the out-of-plane bending deformation of the molecular skeleton caused by the repulsive nonbonded 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.



4 ; R_1 = t-Bu, R_2 = H
5 ; R_1 = H, R_2 = t-Bu

6 ; R_1 = t-Bu, R_2 = H
7 ; R_1 = H, R_2 = t-Bu

8a ; R_1 = t-Bu, R_2 = H
9a ; R_1 = H, R_2 = t-Bu

8b ; R_1 = t-Bu, R_2 = H
9b ; R_1 = H, R_2 = t-Bu

1 ; R_1 = t-Bu, R_2 = H
2 ; R_1 = H, R_2 = t-Bu

Scheme 1.

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 benzocyclopropenecarbaldehyde[3] 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.

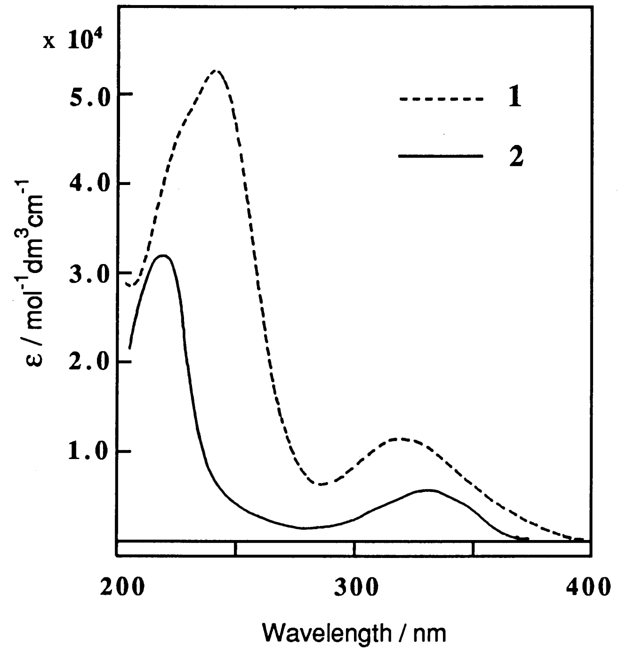
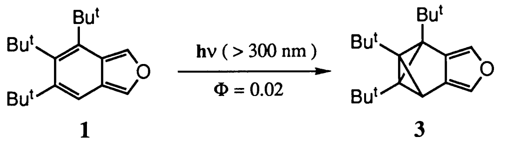


Fig. 1. Electronic spectra of **1** and **2** in acetonitrile.



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-one[6] 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; ^{1}H NMR ($CDCl_3$) 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 $C_{22}H_{34}O_4$: 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; ^{1}H NMR ($CDCl_3$) 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 $C_{22}H_{34}O_4$: 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 tempeprature. 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; ^{1}H NMR ($CDCl_3$) δ=6.99 (1H, s), 5.01 (2H, ABq, *J*=12.5 Hz),[9] 4.66 (2H, ABq, *J*=12.2 Hz),[9] 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 $C_{20}H_{34}O_2$: 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; ^{1}H NMR ($CDCl_3$) 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 $C_{20}H_{34}O_2$: 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 complex[8] 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. ^{1}H NMR (CD_3CN) 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-),[10] 5.47—5.06 (2H, m, -CH_2-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, -CH_2-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; ^{1}H NMR (CD_3CN) 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 $C_{20}H_{30}O$: 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. ^{1}H NMR ($CDCl_3$) 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; ^{1}H NMR (CD_3CN) 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 ^{1}H 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: ^{1}H 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.

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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.