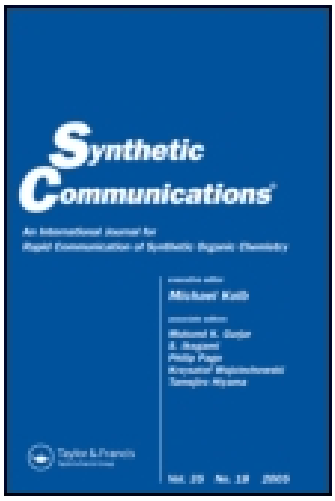

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Synthesis and Characterization of Homologue of Irganox 1076—Some Novel Observations

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Synthesis and Characterization of Homologue of Irganox 1076—Some Novel Observations

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ABSTRACT

A convenient and high yielding preparation of Irganox 1076 homologue from 2,6-di-*tert*-butyl phenol is reported. 2,6-Di-*tert*-butyl phenol on Friedel–Crafts succinoylation in the presence of aluminium chloride leads to migration and elimination of *tert*-butyl group without *tert*-butyl acceptor along with *O*- and *C*-succinoylated products.

Key Words: Antioxidants; De-*tert*-butylation; Isomerization; Succinolyation.

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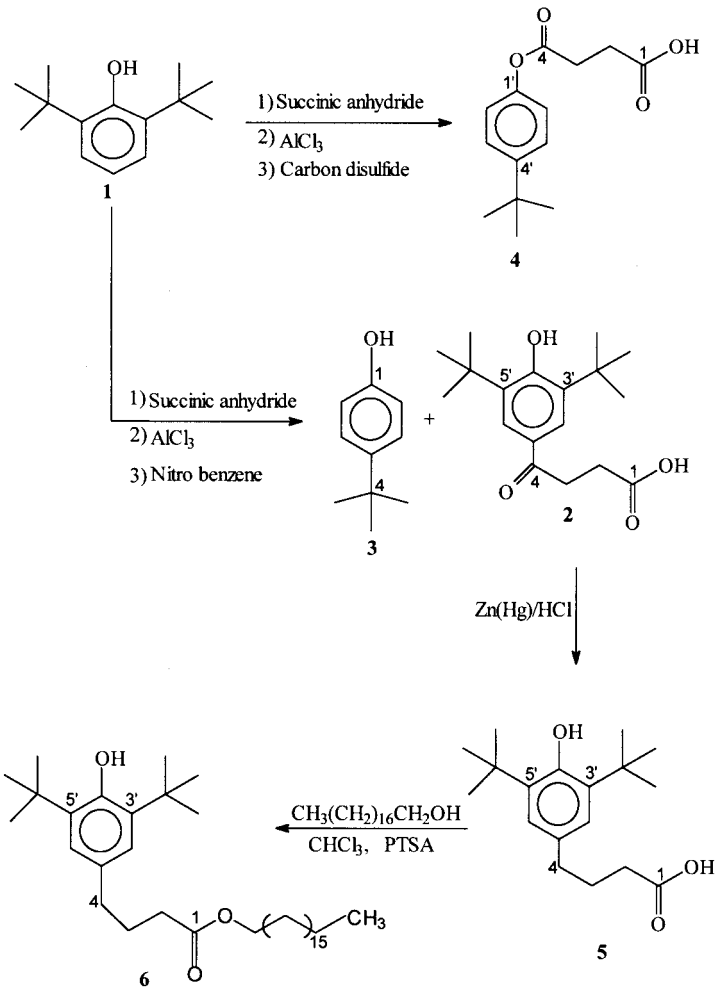
Antioxidants based on hindered phenols are of great importance because of their multiple applications ranging from foods to fuels, plastics as well as ultraviolet absorbing agents.[1] Among these, butylated hydroxy toluene, *tert*-butyl hydroquinone and their derivatives such as octadecyl-3-(3′,5′-di-*tert*-butyl-4′-hydroxy phenyl) propionate (Irganox 1076), are of great interest because of their extensive use in food packaging, pharmaceutical formulations, and polymer stabilization.



Scheme 1.

There are reports in literature regarding the Lewis acid catalysed Friedel–Crafts isomerization[2] and de-*tert*-butylation.[3] The de-*tert*-butylation is also catalysed by metal oxide[4] and mineral acids.[5] Normally de-*tert*-butylation involves the treatment of *tert*-butyl arenes with Lewis acid in the presence of *tert*-butyl acceptor.[6] De-*tert*-butylation of phenols without *tert*-butyl acceptor using TFA is also known, but it involves harsh conditions.[7] Migration or isomerization of alkyl group from one position in the ring to another position in the same ring is known to occur via 1,2 shifts. Any 1,3 or 1,4 shift takes place by series of two or more 1,2 shifts.[8] The literature survey reveals that intramolecular isomerization and de-*tert*-butylation without *tert*-butyl acceptor on a single molecule are novel.

We report a convenient method of synthesis of homologue of Irganox 1076 by introducing one more methylene group in the alkyl chain. This synthesis was achieved by the application of Friedel–Crafts succinoylation on 2,6-di-*tert*-butyl phenol followed by Clemmenson reduction and subsequent esterification of the acid formed.

During the Friedel–Crafts succinoylation we observed de-*tert*-butylation involving carbon–carbon bond rupture without *tert*-butyl acceptor, isomerization of the *tert*-butyl group from the 1,2 position in phenol ring to the 1,4 position in the same ring along with *O*- and *C*-succinoylation. 2,6-Di-*tert*-butyl phenol on Friedel–Crafts succinoylation in the presence of anhydrous $AlCl_3$ in nitrobenzene as solvent gave the desired *C*-succinoylated product **2** along with de-*tert*-butylated and isomerized product **3**. The reaction performed under similar experimental conditions using CS_2 as solvent afforded product **4** due to de-*tert*-butylation, isomerization, and *O*-succinoylation. The keto acid **2** on Clemmenson reduction yielded 4-(3′,5′-di-*tert*-butyl-4′-hydroxy phenyl) butanoic acid **5**, which on esterification with stearyl alcohol gave the desired octadecyl-4-(3′,5′-di-*tert*-butyl-4′-hydroxy phenyl) butanoate **6** (Sch. 1).

EXPERIMENTAL

IR spectra were recorded on Perkin–Elmer IR-781 spectrophotometer. ^{1}H NMR spectra were determined on Brucker-200 MHz ($CDCl_3$/TMS) spectrophotometer and CMR spectra were recorded on Bruker-50 MHz ($CDCl_3$/TMS) spectrophotometer. Elemental analyses were carried out on Coleman C, H analyser.

Friedel–Crafts Succinoylation on 2,6-Di-*tert*-butyl Phenol

To the stirring solution of 2,6-di-*tert*-butyl phenol (0.01 mol) and succinic anhydride (0.015 mol) in nitrobenzene (50 mL), $AlCl_3$ (0.02 mol) was added in parts at temperature 0–5°C. The reaction mixture was stirred for 6 h by keeping the same temperature. The mixture was decomposed with cold water (40 mL) and HCl (10 mL). Nitrobenzene layer was washed with water (5×30 mL) and was removed using Dean-Stark apparatus. The dark brown pasty mass was stirred with Pet. ether (5 mL) and the solid obtained was crystallized from the mixture of benzene and Pet. ether to get compound **2** in 55% yield. Compound **3** was isolated from the surface of the Dean-Stark apparatus and was crystallized using Pet. ether in 10% yield (Path A).

The Friedel–Crafts succinoylation was performed using CS_2 instead of nitrobenzene as solvent under same experimental conditions. The mixture was decomposed in cold water (40 mL) and HCl (10 mL) and carbon disulfide was removed by simple distillation. The pasty mass obtained was stirred with Pet. ether. The solid obtained on crystallization from Pet. ether gave 4′-*tert*-butyl-3-carbophenoxy propanoic acid **4** in 40% yield (Path B).

Synthesis of 4-(3′,5′-Di-*tert*-butyl-4′-hydroxyphenyl) Butanoic Acid

To a solution of keto acid **2** (0.01 mol) in toluene (25 mL), a freshly prepared mixture of amalgamated zinc (from mossy zinc), water (20 mL) and conc. HCl (20 mL) was added. The resulting mixture was refluxed vigorously for 12 h with 5 mL portion of HCl being added every 4 h. After cooling toluene layer was separated and washed with water (3×30 mL). Product obtained after removal of toluene was dried and crystallized from Pet. ether in 90% yield.

Synthesis of Octadecyl-4-(3′,5′-di-*tert*-butyl-4′-hydroxyphenyl) Butanoate

Butanoic acid **5** (0.01 mol) was dissolved in chloroform (50 mL). To this octadecyl alcohol (0.01 mol) was added followed by catalytic amount of PTSA. The reaction mixture was refluxed for 6 h using Dean Stark apparatus and the chloroform was removed by distillation. The crude product was chromatographed over silica gel column using Pet. ether

as eluent to isolate ester **6** as liquid in 84% yield $R_f = 0.81$ (EtoAc–Pet. ether, 1:9).

PHYSICAL DATA AND SPECTRAL CHARACTERIZATION

Compound 2: M.p. 164–165°C (lit[9] 163–165°C). Elemental analysis (%) found for M.F. $C_{18}H_{26}O_4$: C, 71.00; H, 8.09; Calcd: C, 70.59; H, 8.50. IR (KBr) 3520, 3120, 1720, 1705, 1690 cm^{-1}. ^1H NMR: δ_H: 1.46 (18H, s, $2 \times C(C\underline{H}_3)_3$), 2.78 (2H, t, $J = 6.46$ Hz, CH_2), 3.28 (2H, t, $J = 6.46$ Hz, CH_2), 5.73 (1H, s, O<u>H</u>), 7.86 (2H, s, aromatic).

Compound 3: M.p. 95–97°C (lit[10] 96–98°C). Elemental analysis (%) found for M.F. $C_{10}H_{14}O$: C, 79.49; H, 8.94; Calcd: C, 80.00; H, 9.33. IR (KBr) 3240 cm^{-1}. ^1H NMR: δ_H: 1.29 (9H, s, $C(C\underline{H}_3)_3$), 4.60 (1H, s, O<u>H</u>), 6.75 (2H, dd, $J_{5\text{-}6} = 8.7$ Hz and $J_{2\text{-}6} = 1.9$ Hz, aromatic C_5, C_6), 7.30 (2H, dd, $J_{2\text{-}3} = 8.7$ Hz and $J_{3\text{-}5} = 2.1$ Hz, aromatic C_2, C_3). ^{13}C NMR: δ_C: 154 (C_1), 144 (C_4), 127 ($C_{3\text{-}5}$), 115.4 ($C_{2\text{-}6}$), 34.76 ($\underline{C}(CH_3)_3$), 32.31 (CH_3). DEPT indicates the presence of three methyl groups, two different aromatic methine groups, two different quaternary aromatic carbon atoms and one quaternary aliphatic carbon atom.

Compound 4: M.p. 88–90°C. Elemental analysis (%) found for M.F. $C_{14}H_{18}O_4$: C, 67.6; H, 7.33; Calcd: C, 67.2; H, 7.20. IR (KBr) 3120, 1730, 1710, 1700 cm^{-1}. ^1H NMR: δ_H: 1.30 (9H, s, $C(C\underline{H}_3)_3$), 2.85 (m, 4H, CH_2-CH_2), 7.0 (2H, dd, $J_{5'\text{-}6'} = 8.7$ Hz and $J_{2'\text{-}6'} = 2.0$ Hz, aromatic $C_{5'}$, $C_{6'}$), 7.38 (2H, dd, $J_{2'\text{-}3'} = 8.7$ Hz and $J_{3'\text{-}5'} = 1.9$ Hz aromatic $C_{2'}$, $C_{3'}$). ^{13}C NMR: δ_C: 178.01 (CO), 170.87 (CO), 148.73 ($C_{3'}$), 148.20 ($C_{2'}$), 126.20 ($C_{1'}$), 120.71 ($C_{4'}$), 34.43 ($\underline{C}(CH_3)_3$), 31.36 (CH_3), 29.07 (CH_2), 28.92 (CH_2). DEPT indicates the presence of three methyl groups, two methylene groups, two different carbonyl groups, two different aromatic methine groups, two aromatic quaternary carbon atoms and one aliphatic quaternary carbon atom.

Compound 5: M.p. 100–102°C (lit[11] 119–119.5°C). Elemental analysis (%) found for M.F. $C_{18}H_{28}O_3$: C, 74.38; H, 9.69; Calcd: C, 73.97; H, 9.58. IR (KBr) 3520, 3118, 1710 cm^{-1}. ^1H NMR: δ_H: 1.43 (18H, s, $C(CH_3)_3$), 1.8 (2H, m, -CH_2-$C\underline{H}_2$-CH_2-), 2.3 (2H, t, -CH_2-), 2.6 (2H, t, -CH_2-), 5.12 (1H, s, OH), 7.0 (2H, s, aromatic).

Compound 6: Elemental analysis (%) found for M.F. $C_{36}H_{64}O_3$: C, 79.21; H, 11.56; Calcd: C, 79.41; H, 11.76. IR (KBr) 3518, 1738 cm^{-1}. ^1H NMR: δ_H: 0.9 (3H, t, -CH_2-$C\underline{H}_3$), 1.0–1.7 (50H, m, -CH_2-CH_2-, including eighteen *tert*-butyl protons), 1.95 (2H, m, -CH_2-$C\underline{H}_2$-CH_2-),

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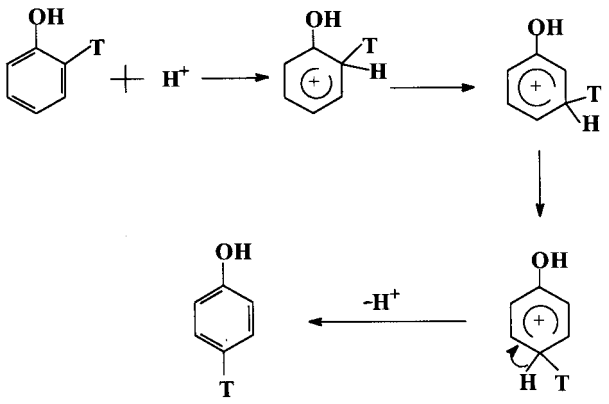
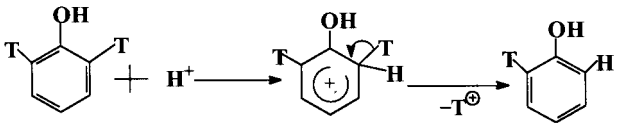
2.35 (2H, t, Ph-$C\underline{H}_2$), 2.6 (2H, t, -CH_2-CO-), 4.1 (2H, t, $COOCH_2$-), 5.01 (1H, s, OH), 7.0 (2H, s, aromatic).

CONCLUSION

This new process for the synthesis of octadecyl-4-(3′,5′-di-*tert*-butyl-4′-hydroxy phenyl) butanoate is convenient, it envisages the use of cheaper starting materials and could be implemented for large scale pre-



Isomerization of tert-butyl group in the presence of acid



De-tert-butylation in the presence of acid

T = Tert- butyl group

Scheme 2.

paration. In the presence of Lewis acid one of the *tert*-butyl group is detached from the aromatic ring and second is isomerized from 1,2 to the 1,4 position in the same ring according to the Sch. 2. In the absence of *tert*-butyl acceptor intra-molecular isomerization was observed. Here as isomerization is fast it is reasonable to suggest that the *tert*-butyl group is not completely detached from the aromatic ring but stays in the interaction through π type of intermediate. Complete detachment of the *tert*-butyl group in alkylation–dealkylation process would be expected to be much slower process.

From the above discussions it is reasonable to say that in case of nitro benzene as solvent, amount of *C*-acylated product is more along with some amount of **3** indicating that de-*tert*-butylation and isomerisation is less in this solvent. The use of carbon disulfide as solvent leads to product **4** in major quantity suggesting that extend of isomerization and de-*tert*-butylation is more in this case.

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