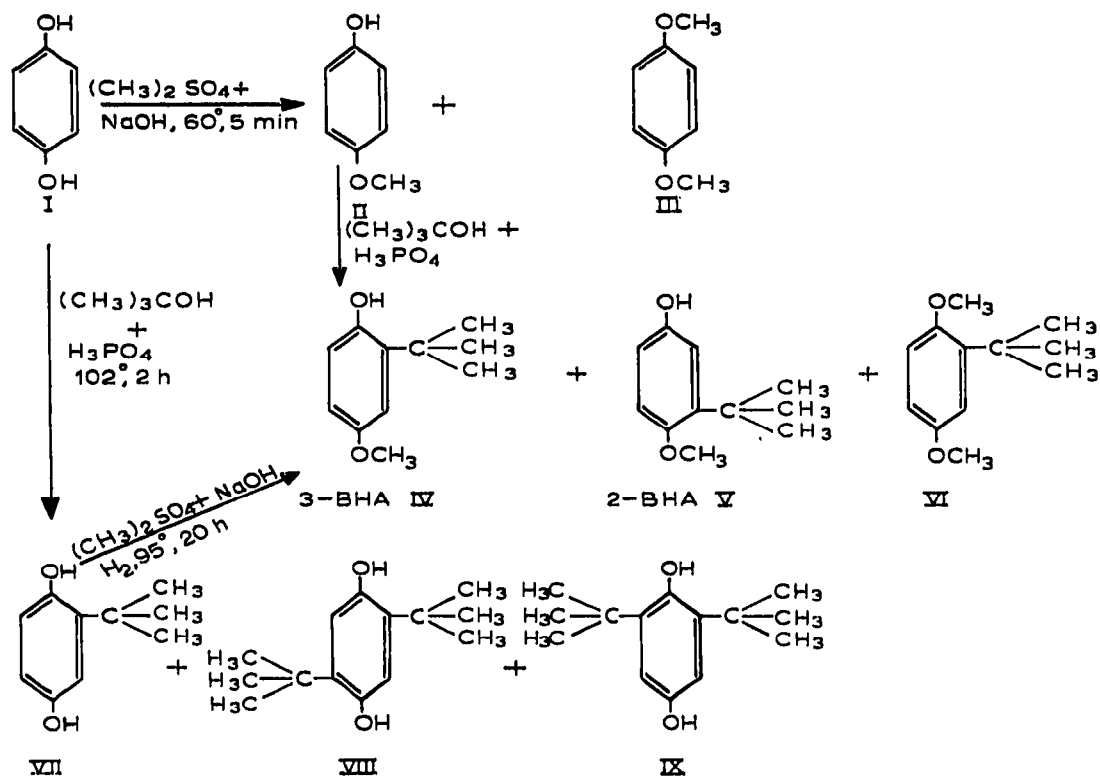


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### Studies on the synthesis of butylated hydroxyanisole

Butylated hydroxyanisole (BHA) is one of the best antioxidants employed for extending the shelf-life of fats and fatty foodstuffs. BHA<sup>1</sup> has better carry-through properties than other known preservatives like butylated hydroxy toluene and alkyl gallates, etc. BHA is either used alone or synergised with alkyl gallates or citric acid.

The two industrial processes employed for the preparation of BHA are: (a) methylation of hydroquinone (I) after the method of ROBINSON AND SMITH<sup>2</sup>, when both *p*-hydroxyanisole (II) and 1,4-dimethoxybenzene (III) are formed. The reaction mass on treatment with *tert.*-butyl alcohol, using phosphoric acid as a condensing agent, gives a mixture of 3-*tert.*-butylhydroxyanisole (IV) and 2-*tert.*-butylhydroxyanisole (V) and 1,4-dimethoxy-*tert.*-butylbenzene (VI). (b) Hydroquinone (I) on butylation gives *tert.*-butylhydroquinone (VII) along with 2,5-di-*tert.*-butylhydroquinone (VIII) and 2,6-di-*tert.*-butylhydroquinone (IX). (VII) on methylation with dimethyl sulphate and aqueous sodium hydroxide in a hydrogen atmosphere (95°, 20 h) gave a mixture<sup>3</sup> of two BHA isomers (IV) and (V) along with (VI).



The yield of BHA is affected by various intermediates, the formation of which depends on different experimental factors like (1) molar concentration of reactants, (2) temperature of reaction, (3) time of reaction, etc. Even the ratio of 3- and 2-isomers of BHA varied between 80–90% and 2–20%, respectively, in the final product. In a continuous process the intermediate byproducts are not separated. In order to get the

required optimum yields of BHA, it becomes essential to identify rapidly and to estimate the various intermediate compounds.

3- and 2-BHA, mono- and di-*tert.*-butylhydroquinones have been investigated by gas chromatography (GC)<sup>4-10</sup>, column chromatography (CC)<sup>11,12</sup>, paper chromatography (PC)<sup>13-21</sup> and thin-layer chromatography (TLC)<sup>22-38</sup>.

The present paper describes a rapid procedure for the separation and estimation of various compounds with only 2  $\mu\text{g}$  formed in different synthetic routes of butylated hydroxyanisole.

### Experimental

*Materials and methods.* The various compounds, *viz.*, *p*-hydroxyanisole (m.p. 53°), 1,4-dimethoxybenzene (m.p. 56°), *tert.*-butylhydroquinone (m.p. 129°)<sup>39</sup>, 2,5-di-*tert.*-butylhydroquinone (m.p. 211-212°)<sup>39,40</sup>, 2,6-di-*tert.*-butylhydroquinone (m.p. 102°)<sup>39</sup>, 3-*tert.*-butylhydroxyanisole (m.p. 62-63°)<sup>41</sup>, 2-*tert.*-butylhydroxyanisole (m.p. 65°)<sup>42</sup> and 1,4-dimethoxy-2-*tert.*-butylbenzene (b.p. at 12 mm 117-118°)<sup>43</sup> were synthesised after standard procedures and purified by subjecting them to vacuum distillation, column chromatography through alumina, and repeated crystallisations with petroleum ether (b.p. 40-60°). The compounds gave single spots on PC and TLC. All solvents were freshly dried and distilled. The temperature of irrigation was  $22 \pm 2^\circ$ . Kodak photographic glass plates (35 × 22 cm) were used. The distance travelled by the solvent front in each case was 30 cm. The compounds were detected by a short-wave UV lamp "Chromatolite". A Hilger UV spectrophotometer was used for recording the percentage transmissions of 75% ethanolic solutions of individual compounds at suitable wavelengths.

*Preparation of thin-layer plates, application of the compounds and irrigation of the plates.* The slurry of the sorbent in chloroform-methanol was poured on the glass plates. The plates were dried at room temperature overnight and heated at  $120 \pm 2^\circ$  in an oven for  $\frac{1}{2}$  h before use. The plates were weighed before spotting, and average coating of the sorbent was recorded. The average coatings of sorbents (mg/cm<sup>2</sup>) in the cases of Kieselgel G (Merck), neutral alumina with 20% CaSO<sub>4</sub> (Woelm, 200 mesh, B.S.S.), Kieselgel G + Kieselguhr G (75:25) were 7.2, 6.8 and 7.5, respectively.

An acetone solution of each standard sample (2  $\mu\text{l}$  containing 2  $\mu\text{g}$ ) was spotted on the chromatoplates, 10  $\mu\text{l}$  of the acetone solutions of the reaction products from processes (a) and (b) were also applied. The plates were irrigated with suitable solvents employing the ascending technique. The plates were viewed under UV light and migrations of compounds were noted. Fig. 1 is a typical chromatoplate showing the resolutions of various compounds formed during the preparation of BHA by synthetic routes (1) and (2). Table I gives the  $R_F$  values of various compounds.

*Quantitative analysis.* The individual compounds separated from different reaction products were scraped with a microspatula on a sintered funnel and extracted with 75% ethanol to obtain a known volume. The percentage transmissions were recorded against suitable wavelengths: hydroquinone, 299  $m\mu$ ; *p*-hydroxyanisole, 243  $m\mu$ ; 1,4-dimethoxybenzene, 290  $m\mu$ ; *tert.*-butylhydroquinone, 245  $m\mu$ ; 2,5-di-*tert.*-butylhydroquinone, 294  $m\mu$ ; 2,6-di-*tert.*-butylhydroquinone, 288  $m\mu$ ; 3-*tert.*-butylhydroxyanisole, 291  $m\mu$ ; 2-*tert.*-butylhydroxyanisole 242  $m\mu$ ; 2-*tert.*-butyl-1:4-dimethoxybenzene, 288  $m\mu$ . The amounts of each compound were calculated from the standard curves previously plotted for the individual compound.

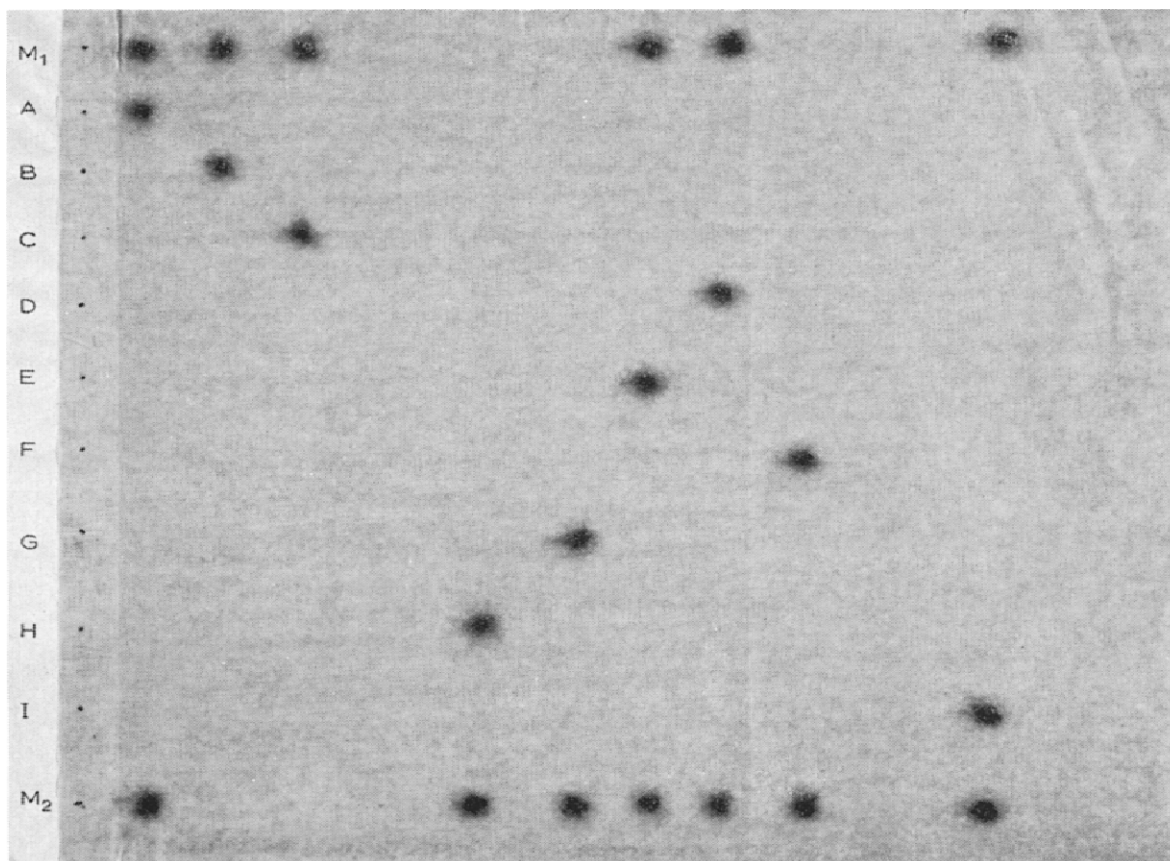


Fig. 1. Thin-layer chromatogram showing the resolutions of various compounds formed during the synthesis of butylated hydroxyanisole (BHA).  $M_1$  = product from reaction (a); A = hydroquinone; B = *p*-hydroxyanisole; C = 1,4-dimethoxybenzene; D = 3-BHA; E = 2-BHA; F = *tert.*-butylhydroquinone; G = 2,6-di-*tert.*-butylhydroquinone; H = 2,5-di-*tert.*-butylhydroquinone; I = 1,4-dimethoxy-*tert.*-butylbenzene;  $M_2$  = product from reaction (b). Sorbent: Kieselgel G. Solvent: chloroform-cyclohexane (1:1). Development: ascending.

### Results and discussion

Hydroquinone was strongly adsorbed. Methylation of the hydroxyl group helps in the migration; thus *p*-hydroxyanisole was more mobile than hydroquinone and dimethoxybenzene had a higher  $R_F$  value than *p*-hydroxyanisole. Substitution of the *tert.*-butyl group in hydroquinone helps its mobility. 2,5-Di-*tert.*-butylhydroquinone had a lower  $R_F$  value than the 2,6-isomer. This was due to complete masking of one hydroxyl group by two *tert.*-butyl groups in the latter compound and thus helping in its mobility. 3-BHA migrated further than 2-BHA. It is observed that a compound with two electron-donating groups in vicinal positions in an aromatic ring will have a longer migration than the *meta*-substituted compound.

The compounds could be conveniently extracted with aqueous ethanol in the cold and the percentage transmissions at their respective maxima could be easily recorded, thus enabling quick estimations of all the compounds formed in the synthesis of butylated hydroxyanisole.

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TABLE I  
*R<sub>F</sub>* VALUES OF VARIOUS COMPOUNDS FORMED DURING THE SYNTHESIS OF BHA

Serial No.	Compound	Sorbents/solvents								
		Kieselgel G		Neutral alumina-calcium sulphate (80:20)		Kieselgel G-Kieselgel G (3:1)				
		Cyclo-hexane-dioxane	Benzene	Chloroform-cyclohexane (1:1)	Petroleum ether-dioxane (9:1)	Petroleum ether-cyclohexane (1:1)	Chloroform-cyclohexane (1:1)	Cyclo-hexane-dioxane (9:1)	Chloroform-cyclohexane (2:3)	Chloroform-petroleum ether (2:3)
1	Hydroquinone	0.11	0.03	0.05	0.09	0.00	0.02	0.06	0.04	0.03
2	<i>p</i> -Hydroxyanisole	0.19	0.13	0.12	0.28	0.20	0.10	0.21	0.21	0.14
3	1,4-Dimethoxybenzene	0.36	0.23	0.20	0.42	0.43	0.31	0.30	0.41	0.40
4	3- <i>tert.</i> -Butylhydroxyanisole	0.62	0.53	0.61	0.81	0.21	0.47	0.52	0.38	0.37
5	2- <i>tert.</i> -Butylhydroxyanisole	0.57	0.49	0.54	0.76	0.09	0.42	0.48	0.31	0.33
6	2- <i>tert.</i> -Butylhydroquinone	0.80	0.63	0.69	0.92	0.62	0.92	0.72	0.79	0.84
7	2,6-Di- <i>tert.</i> -butylhydroquinone	0.94	0.90	0.47	0.64	0.76	0.79	0.92	0.75	0.71
8	2,5-Di- <i>tert.</i> -butylhydroquinone	0.54	0.75	0.39	0.26	0.70	0.50	0.81	0.68	0.63
9	1,4-Dimethoxy-2- <i>tert.</i> -butylbenzene	0.90	0.69	0.86	0.90	0.83	0.96	0.76	0.80	0.82

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