Organic Reaction in Liquid Hydrogen Fluoride. V. Reactions and Formation of *tert*-Butylphenols

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In temperature ranges of −75 to 100° *o*-, *m*-, and *p*-*tert*-butylphenols (TBP) isomerize and disproportionate in liquid hydrogen fluoride to varying extents depending on the temperature. At −40° the ortho isomer is isomerized exclusively to the para isomer. Above 0° the meta isomer tends to predominate and reaches a maximum of 86% of the total monoalkylated fraction beginning with *o*- or *p*-TBP. At 30–75° transalkylation to phenol and di-TBP occurs with the 3,5-di-TBP being preferentially formed. Above 75° extensive degradation of the molecule occurs with phenol and heavy tars being formed. Phenol is alkylated with isobutylene using catalytic amounts of HF to form the *p*-TBP and 2,4-di-TBP at 25°, but if solvent quantities of HF are used the *m*- and 3,5-di-TBP are obtained.

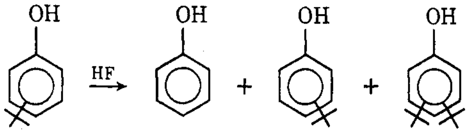
In the preceding paper[1] the Fries rearrangement of substituted phenyl benzoates was discussed. It was shown that when *tert*-butyl groups are on the phenolic ring there is a tendency toward dealkylation. Depending on the ring position, this dealkylation may be very extensive. For example, *p*-*tert*-butylphenyl benzoate gave only dealkylated *p*-hydroxybenzophenone, whereas the meta isomer gave a 40% yield of the Fries product, 2-hydroxy-4-*tert*-butylbenzophenone. We now make similar observations for the free *tert*-butylphenols (TBP), since the most stable TBP in liquid HF is the meta isomer. Also to be expanded in this report is the fact that the 3,5-di-TBP is the most stable disubstituted isomer and that alkylation of phenol with isobutylene in liquid HF can give both *m*-mono- and 3,5-di-TBP instead of the classical ortho and para derivatives.

The literature reports considerable work on reactions of *tert*-butylphenols with various acid catalysts, but no reports could be found in which HF alone was employed.[2] In an excellent study on isomerization of *tert*-butylphenols, Bolton, *et al.*,[3] using type Y zeolite catalysts at 100–200°, found that isomerization is always accompanied by transalkylation. The equilibrium distributions at 200° are approximately 1% ortho, 72% meta, and 25% para in the monophenol fraction with the dialkyl fraction consisting of 2% 2,6-, 83% 3,5-, 5% 2,4-, and 10% 2,5-di-TBP. These workers further demonstrated that the formation of the meta derivatives is attributable to the transalkylation of the ortho and para phenols and not to direct alkylation.

Formation of meta-substituted *tert*-butylphenols from a preparative viewpoint was first reported by Olin,[4] who isomerized *p*-TBP to a mixture containing the meta isomer over a catalyst of sulfuric acid supported on an activated clay. Later Bondy and Moore[5] obtained *m*-TBP from a mixture of *o*- and *p*-TBP on a similar type of catalyst. However, until the recent work by Bolton, *et al.*,[3] no careful study of the isomerization and transalkylation of *tert*-butyl phenols had been carried out. Thus we have investigated this isomerization in liquid HF at much lower temperatures than those for the zeolite work.

Results

Hydrogen fluoride functions as an excellent catalyst–solvent system for studying phenols in that it is nonoxidizing, is a very strong acid ($H_0 = -10$), and possesses a low boiling point (20°) to facilitate easy removal. The work involved dissolving each of the three mono-*tert*-butylphenols in liquid HF at temperatures from −75 to 100° for 2 hr. As shown in Table I, varying ratios of phenol, mono-*tert*-butylphenols, and di-*tert*-butylphenols were isolated by quenching the mixtures with ice followed by ether extraction after neutralization. The product distribution was determined by glc methods using the silylated derivatives (see Experimental Section). Especially at higher temperatures, large amounts of "heavies" attributable to polyalkylated phenols and butylated oligomers were observed. The quantities of these materials were determined by use of an internal standard in the glc determination; the data in Table I are normalized to provide a ready visual comparison of the relative reactivities.



Pertinent observations gleaned from the results in Table I are as follows. (1) The ortho and para isomers at 30° tend toward the same equilibrium ratio in the monoalkyl fraction of approximately 85% *m*- and 15% *p*-TBP with none or traces of the ortho isomer being observed. This is roughly similar to the equilibrium values obtained by Bolton[2] working at 200° with zeolites. The meta isomer shows only a slight alteration, with the distribution being 98% meta and 2% para, indicating its higher stability. (2) At −75° there is essentially no isomerization and at 100° the molecule is greatly degraded with the principal product being phenol and unidentified oligomers. This effect is independent of the starting isomer. (3) A novel phenomenon occurs with the ortho isomer at −40° in that complete conversion to *p*-TBP is realized. The

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[1] J. R. Norell, *J. Org. Chem.*, **38**, 1924 (1973).

[2] A recent review article entitled "Unusual Electrophilic Aromatic Substitutions in Synthesis," by D. E. Pearson and C. A. Buehler, *Synthesis*, 474 (1971), cites use of HF in a table for the transformation of 4-TBP to 3-TBP, but, on careful inspection of the original work, a Ph.D. thesis by R. Wysong, Vanderbilt University, 1967, p 40, it is revealed that actually a mixture of HF and BF_3 was used.

[3] A. P. Bolton, M. A. Lanewala, and P. E. Pickert, *J. Org. Chem.*, **33**, 3415 (1968).

[4] J. F. Olin (to Pennsalt Chemical Corp.), U. S. Patent 3,014,079 (Dec 19, 1961).

[5] M. F. Bondy and F. R. Moore (to Coalite and Chemical Products Ltd.), British Patent 992,629 (May 19, 1965).

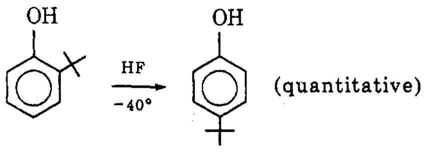
TABLE I

tert-BUTYLPHENOL ISOMERIZATION IN LIQUID HF[a]

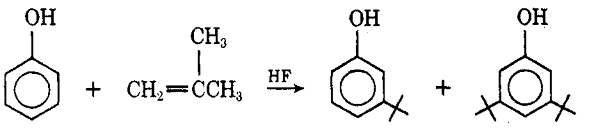
tert-Butylphenol	Temp, °C	Amount recovered, %	Heavies, %	Phenolic distribution, wt %: Phenol	Mono-TBP	Di-TBP[c]	Distribution of mono-TBP, %: Ortho	Meta	Para
ortho	−75	95	0	2	92	6	98	0	2
ortho	−40	93	0	3	97	0	0	0	100
ortho	−5	93	Tr	10	77	13	0	19	81
ortho	30	95	3	24	24	52	0	86	14
ortho	55	83	8	32	22	46	1	80	19
ortho	75	90	19	42	25	33	6	74	20
ortho	100	81	41	89	8	2	27[b]	73[b]	0
meta[d]	−75	83	0	0	100	0	0	91	9
meta	−40	91	0	3	97	0	0	97	3
meta	−5	93	0	5	87	8	0	97	3
meta	30	96	Tr	12	61	27	0	98	2
meta	55	91	3	25	18	57	0	86	14
meta	75	93	11	30	24	46	0	83	17
meta	100	83	28	100	Tr	0	0	53[b]	47[b]
para	−75	94	0	0	100	0	0	0	100
para	−40	91	0	2	98	Tr	0	0	100
para	−5	93	Tr	9	77	14	0	18	82
para	30	94	22	26	22	52	0	86	14
para	55	91	30	37	22	41	2	84	14
para	75	100	35	45	23	32	3	80	17
para	100	79	22	88	12	0	74[b]	0	26[b]

[a] All runs were made with 15 g (0.10 mol) of *tert*-butylphenol in 100 ml of HF for 2 hr. [b] Where the amount of mono-*t*-BuPhOH is low, the distribution of ortho–meta–para is probably meaningless. [c] The dialkylated phenol is chiefly the 3,5 isomer. [d] Starting purity of *m*-*tert*-butylphenol was 91% meta and 9% para.

reaction is so "clean" that from the liquid ortho isomer, which readily dissolves in HF, the white crystalline para isomer is recovered nearly quantitatively. Further rearrangement, however, occurs as the temperature is increased. (4) Purchased *m*-TBP contained 9% of the para isomer, which was not easily removed by distillation. Increased purity is attained when the 91:9 mixture is placed in HF at 0–30°, since the purity of the monoalkyl fraction increases to 98.2% meta and 1.8% para. (5) The major constituent (>95%) of the dialkylated phenol is the 3,5-di-TBP. This represents a much larger amount than that observed over the zeolites.[2] This material arises *via* a transalkylation step and the method can serve as a synthesis for the 3,5 isomer starting with any of the mono-TBP. The amount of 3,5-di-TBP reaches a maximum of 40–50% at temperatures of 30–50°. Above these temperatures even the most stable 3,5 isomer tends to dealkylate and at 100° phenol *per se* is the chief volatile constituent. Even though the yield of 3,5-di-TBP is only moderate the method is superior to the original, but recent, synthesis which involves four steps.[6] Generally in the preparation of dialkylated phenols the ortho and para isomers, *i.e.*, 2,4-di-TBP, are those expected under normal alkylation conditions, or the 2,6-di-TBP can be obtained using aluminum phenoxide.[7]



In spite of literature reports[8] that phenol is never alkylated in the meta position, the above data on stabilities of *tert*-butyl groups suggested that meta-substituted products could be isolated under alkylation-type conditions, *i.e.*, reaction of isobutylene with phenol in HF. Indeed it was found that, if phenol is alkylated with isobutylene in solvent quantities of HF, *m*-TBP and 3,5-di-TBP are the principal phenols.



A summary of the data (Table II) collected indicates that *p*-TBP forms first and then it isomerizes and transalkylates to the *m*-TBP or 3,5-di-TBP. Preparatively, the method is fair (30% yield) for producing 3,5-di-TBP by direct alkylation because butylene oligomers form in a competing reaction. The reaction is best carried out with a small amount of HF catalyst at 25° to effect the "classical" alkylation in the ortho and para positions. The mixture is cooled and solvent quantities of HF are added so as to effect the isomerization and transalkylation to form the thermodynamically most stable isomers. An alternative method for synthesis of the 3,5 isomer involves the alkylation of *m*-TBP with isobutylene at 0° in 100 ml of HF, which gives a phenolic mixture of 50% 3,5-di-TBP, 7% *p*-TBP, and 43% unreacted *m*-TBP.

When other *tert*-butyl carbonium ion precursors are used, *i.e.*, *tert*-butyl alcohol and *tert*-butyl chloride, the yields are similar except that in the latter case the para isomer predominates, which is probably due to the lower temperature of reaction (Table II). Alkylation

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(6) J. W. Elder and R. P. Mariella, *Can. J. Chem.*, **41**, 1653 (1963).

(7) L. F. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold, New York, N. Y., 1961, p 760.

(8) J. H. Patinkin and B. S. Friedman, "Friedel-Crafts and Related Reactions," Vol. II, Part I, G. A. Olah, Ed., Interscience, New York, N. Y., 1964, pp 75–77.

TABLE II

ALKYLATION OF PHENOL WITH ISOBUTYLENE IN HF

Run	Phenol, mol	Isobutylene, mol	HF, ml	Temp, °C	Time, hr	Product distribution (normalized)[a] Phenol	m-TBP	p-TBP	3,5-Di-TBP	2,4-Di-TBP	Comments
1	0.20	0.64	100	−70	0.7	1	0	35	0	64	C_4H_8 was bubbled in over a period of 1 hr
2	0.20	0.59	130	−78	2	4	0	80	0	17	A mixture of phenol in HF was added to a mixture of C_4H_8 in HF at −78°
3	0.20	0.23	100	0	2	5	11	61	20	3	C_4H_8 was bubbled in over a 2-hr period
4	0.20	0.40	125	−78 to 55	2	50	20	3	27	0	Run as in run 2 except warmed to 55°
5	0.10	0.20	104	−78 to 25	2	31	18	28	21	2	Phenol and 4 ml of HF were mixed at −78°, C_4H_8 was added and allowed to mix for 1 hr; 100 ml of HF was added, stirred for 1 hr at 78°, then warmed to 25°
6	0.16	0.20	104	−78 to 25	3	22	18	13	47	0	Phenol and 4 ml of HF were mixed at 78°, C_4H_8 was added and the reactor was shaken at 25° for 1 hr. A rapid exotherm occurred at 25-45°. After cooling to −78° 100 ml of HF was added and the mixture was again warmed to 25° for 2 hr
7	0.16	0.45	100	−70 to 25	2	28	13	48	11	0	Reactants were mixed at −78° and allowed to warm to 25°
8	0.20	0.40[b]	100	55	2	38	26	10	26	0	
9	0.10	0.20[c]	100	0	2	3	14	60	23	0	
10	0.24	0.49	10 g[d]	150	2	30	8	40	0	22	Benzene (50 ml) was used in a solvent

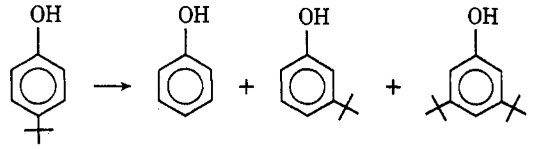
[a] Depending on the amount of excess isobutylene, the oligomer found varied to as much as 30%; therefore, the phenolic distribution has been normalized. [b] *tert*-Butyl alcohol was used in place of isobutylene. [c] *tert*-Butyl chloride was used in place of isobutylene. [d] Zeolon H, an acidic molecular sieve from Norton Chemical Co. which had been treated at 600° for 4 hr, was used in place of HF.

of phenol with isobutylene employing an acidic zeolite, Zeolon H, at 150° in benzene gave very little *m*-TBP and no detectable 3,5-di-TBP; *p*-TBP and 2,4-di-TBP were the chief products. Zeolon H is probably a much less acidic zeolite than the type Y used by Bolton, *et al.*,[3] and hence no meta isomers were produced.

Discussion

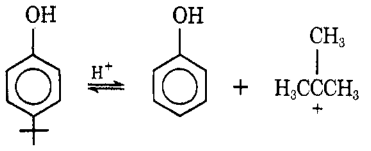
The kinetic experiments of Bolton, *et al.*, over zeolites at 200° coupled with our observations over a wide temperature range in liquid HF support the concept that isomerization of *tert*-butylphenols proceeds *via* a transalkylation mechanism rather than an intramolecular rearrangement.

For *p*-TBP the chief products found are as follows.

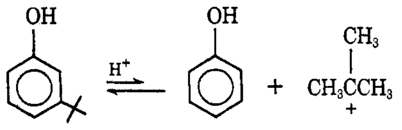


The meta derivatives tend to be more stable because during protonation of the phenol the meta position is less vulnerable to dealkylation, as presented in our previous paper.[1] Other than the 3,5 isomer, very little of the other dialkylated phenols are observed in liquid HF. This may be due to the fact that each experiment is run exhaustively rather than kinetically as reported for the zeolite case.[3]

The observation that the meta isomer is preferentially formed in solvent quantities of HF whereas the para isomer is the chief product when catalytic amounts of HF are employed during alkylation of phenol with isobutylene is best rationalized on an understanding of the reversibility of the reaction. In essence *p*-TBP and *o*-TBP, when placed in solvent quantities of HF, react reversibly as follows.



With the meta derivative this equilibrium lies much further to the left. Thus the *tert*-butyl carbonium ion



can attack in the ortho or para position or lose a proton forming an olefin, which is the equivalent of adding isobutylene to the reaction. Oligomers can be formed that utilize the *tert*-butyl carbonium ion. However, once attack occurs in the meta position reversibility is much less pronounced and hence a build-up of the meta isomer is observed. The same holds true for the 3,5-di-TBP. With catalytic amounts of catalyst the initial attack is at the electron-rich ortho and para centers and since insufficient HF is present for cleavage of the *tert*-butyl group, the para and 2,4 isomers are those isolated. Although some reports have been found for the formation of ortho derivatives and ethers in alkylation with acids,[8] we were unable to find any such materials in the reaction in HF. The rapid interconversion of ortho to para at −40° probably accounts for such observations.

Experimental Section

Apparatus.—All reactions above 0° were carried out in a 300-ml Monel vessel equipped with a pressure gauge and Hoke valves. Heating and mixing were supplied by shaking the reactor in an Eberbach thermostated reciprocating shaking water bath. For reactions at 0° and lower a polyethylene vessel was constructed (450-ml capacity) with two openings so that a thermometer could be inserted into the liquid. The reactor was placed in a coolant at the desired temperature and magnetically stirred.

Chemicals.—Hydrogen fluoride was obtained from Air Products Co. It was withdrawn in the liquid phase and was used directly without further purification. Note precautions to be observed when using HF.[1] All the *tert*-butylphenols (TBP) were obtained from Aldrich Chemical Co. The para isomer was used as received and the ortho and meta isomers were distilled prior to usage. Even after distillation, the composition of the latter was 91% *m*- and 9% *p*-TBP.

Analytical Procedure.—A variety of gas chromatographic procedures was employed throughout the course of this work for analyses of phenol, and the mono- and di-*tert*-butylphenols, with the most satisfactory method being described below. A total determination is based on a combination of glc chromatograms on both silylated and nonsilylated phenols using a Hewlett-Packard Model 5752-B gas chromatograph (T. C. cells). The column used was based on work by Duvall and Tulley[9] and consisted of a 60:40 mixture of silicone 550 and Carbowax 20M on silanized (DMCS) Chromosorb W, acid-washed, 60/80 mesh, packed in a 10 ft × 0.25 in. stainless steel column. Loading of the liquid phase was 9% on the support for the silylated samples and 17% for the free phenols. Samples were silylated with Regisil, *N,O*-bis(trimethylsilyl)trifluoroacetamide from Regis Chemical Co., 100–200-mg sample/1 ml Regisil, and column conditions were as follows: 3-min postinjection period, programmed from 140° to 165° at 10°/min, held for 20 min.

Under these conditions, the following elution times were observed for the silylated derivatives (Table III).

TABLE III

Component	Retention time, min:sec	Correction factors
Phenol	4:10	0.92
o- and *m*-TBP	9:25	1.05
p-TBP	10:12	1.05
3,5-di-TBP	14:55	1.17
2,4-di-TBP	16:45	1.17
2,5-di-TBP	17:35	1.17

Prior to silylation all the expected components are separable except the meta and para isomers, whereas after silylation the *o*- and *m*-*tert*-butylphenols are not separable. Thus, two chromatograms are required for each sample and the exact amount of each isomer is determined by arithmetic methods. Elution times for the nonsilylated phenols on a similar column except isothermally at 225° gave the following retention times (Table IV).

TABLE IV

Component	Retention time, min:sec	Correction factors
Phenol	4:07	0.92
2,6-di-TBP	6:27	1.00
o-TBP	7:21	1.05
m- and *p*-TBP	9:36	1.05
2,4-di-TBP	12:07	1.00
3,5-di-TBP	16:05	1.17

Quantitative measurements were made by use of a Disc Integrator which gave the number of counts per peak. Correction factors were determined by use of carefully weighed knowns for both the silylated and nonsilylated samples. The percentages of heavies, *i.e.*, butylene oligomers, heavily alkylated phenols, and other material not eluting on the column, were determined by weighing a known amount of *p*-cresol into the sample, as an internal standard, prior to glc analysis. This technique was employed only on nonsilylated samples. The equation from which the percentage of heavies was determined is

$$\%\ \text{heavies} = \frac{\text{wt of sample} - \text{wt of std} \times \dfrac{\text{total peak ct}}{\text{std ct}}}{\text{wt of sample}} \times 100$$

Standard Procedure for Reactions above 0°.—The phenol was placed in a 300-ml Monel reactor cooled in ice under a N_2 flow. Liquid hydrogen fluoride was added, and the reactor was capped and placed in the shaker bath at the desired temperature. After the allotted time, the reactor was cooled, the valve was opened, and the HF was bled off. The reactor was opened and the reaction mixture was poured into ice water, neutralized with $NaHCO_3$, and extracted with ether. After drying over $MgSO_4$–K_2CO_3 mixture, the extracts were concentrated to give the crude phenol mixture as recorded in Table I.

Standard Procedure for Reaction below 0°.—The 450-ml polyethylene reactor containing 100–150 ml of HF was cooled in the suitable collant until the temperature reached that specified. The phenol was added and stirred magnetically for the allotted time. The entire mixture was quickly poured on ice, neutralized with $NaHCO_3$, and extracted with ether. After drying, the extracts were concentrated to give the crude phenol mixtures.

General Procedure for Alkylation Reactions (Table II).—The phenol was placed in either the Monel or polyethylene reactor and HF was cautiously added. The mixture was cooled or heated to the desired temperature and isobutylene or other *tert*-butyl carbonium ion source was added. Isobutylene was usually added slowly through a Gilmont gas flow meter. The reactor was then shaken or stirred at the specified time and temperature. The contents were poured on ice, and ether extracted, and the combined ether extracts were neutralized by shaking with saturated $NaHCO_3$ solution. After drying over $MgSO_4$ and concentration the resulting, usually viscous, residues were analyzed by glc techniques described above. The data displayed in Table II are representative runs of many experiments under a variety of conditions. Because the various methods employed for carrying out the reaction greatly affect the product distribution, a column entitled "Comments" is included in Table II.

Registry No.—Hydrogen fluoride, 7664-39-3; *o*-*tert*-butylphenol, 88-18-6; *m*-*tert*-butylphenol, 585-34-2; *p*-*tert*-butylphenol, 98-54-4; phenol, 108-95-2; isobutylene, 115-11-7.

Acknowledgment.—The helpful discussions with Dr. John E. Mahan and the capable laboratory assistance of Mr. Bill Loffer are gratefully recognized.

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(9) A. H. Duvall and W. F. Tulley, *J. Chromatogr.*, **11**, 38 (1963).