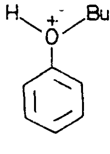
Predominant *O*-alkylation in the Gas-phase Attack of t-Butyl Cations on Phenol and Anisole

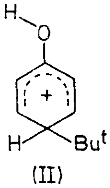
By MARINA ATTINÀ, FULVIO CACACE, GIOVANNA CIRANNI, and PIERLUIGI GIACOMELLO
(*University of Rome*, 00100 *Rome, Italy*)

Summary In the gas-phase attack of t-$C_4H_9^+$ ions, obtained in the dilute gas state from the radiolysis of neopentane, on phenol and anisole, the competition between *n*-type and π-type nucleophilic centres of the ambident substrates is strongly biased in favour of the oxygen atom, leading to the predominant formation of the t-butylated oxonium ions as the major reaction intermediates.

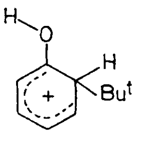
THE competition between *n*- and π-type nucleophilic centres of phenols and aromatic ethers for charged electrophiles has been the subject of extensive investigation, concerning, in particular, protonation and alkylation reactions.[1]



(I)

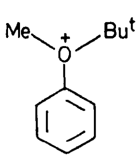


(II)

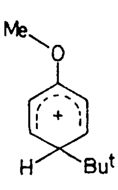


(III)

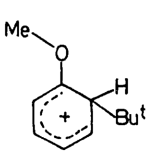
From the available data, the reactivity of the oxygen atom and of the aromatic ring appear sufficiently close to make the ratio of *O*-attack to the *C*-attack critically dependent on the specific reaction environment, in particular on the solvation of the reagents and of the charged intermediates. Under such circumstances, the evaluation of the *intrinsic* reactivity of the two nucleophilic centres would be greatly simplified, and a number of inconsistencies removed, by carrying out the electrophilic substitution in a dilute gaseous system, where the effects of solvation, ion-pairing, *etc.* are eliminated. We have now extended to typical ambident substrates, such as phenol and anisole, the study of gas-phase alkylation by radiolytically formed t-butyl cations; previously such methods have been applied to the determination of the substrate and positional selectivity of t-$C_4H_9^+$ attack on a variety of arenes.[2]



(IV)



(V)



(VI)

The alkylation of phenol and anisole was carried out by irradiating (^{60}Co source; 22 °C) a gaseous system containing neopentane (720 Torr) in the presence of traces (0.02—1·5 Torr) of the aromatic substrate(s), of a radical scavenger (O_2), and of a gaseous base (NH_3). The t-butyl cations, formed in a known yield from the radiolysis of neopentane, are thermally equilibrated by unreactive collisions with neopentane molecules before attacking the aromatic substrate(s).

The oxonium and arenium ions formed from the exothermic alkylation are also stabilized by collision with neopentane molecules, and eventually transfer a proton to a gaseous base, forming the *O*-alkylated and/or *C*-alkylated neutral products, whose identity and yields, determined by g.l.c., are given in the Table. The products were identified by comparison of their retention times, on at least two columns, with those of authentic samples, and their yields were determined from the area of the correspondent elution peaks, using individual calibration factors.

TABLE

Gas-phase competition of phenol (anisole) with toluene for t-$C_4H_9^+$ cations.

System composition,[a] pressure/Torr						Isomeric composition of products[b]			
PhX	PhMe	NH_3	k(PhX)/k(PhMe)	*O*-Alkylation (%)	*C*-Alkylation (%)	Bu^t–C_6H_4–X		Bu^t–C_6H_4–Me	
						o-	*p*-	*m*-	*p*-
X = OH									
0·28	0·81	5	5	85	15	33	67	7	93
0·32	0·75	—	4	79	21	20	80	10	90
X = OMe									
0·72	0·70	—	0·8	—	—	71	29	7	93
1·03	1·10	—	0·8	—	—	74	26	7	93
0·65	0·62	2	1·5	—	—	65	35	6	94
0·02	0·19	5	1·4	—	—	70	30	5	95
1·33	1·47	5	1·1	—	—	70	30	6	94
0·62	0·42	17	1·9	—	—	61	39	6	94
0·69	0·97	23	1·8	—	—	62	38	6	94

[a] Neopentane pressure 720 Torr, O_2 pressure 5 Torr, radiation dose 0·3—2·9 MRad. [b] Standard deviation *ca.* 10%.

The results obtained for the t-butylation of phenol provide direct evidence that the attack of t-$C_4H_9^+$ occurs predominantly (*ca.* 5:1) at the *n*-centre, yielding the oxonium ion (I) as the major product, with much lower amounts of the arenium ions (II) and (III) [*ca.* 2:1 ratio of (II): (III)].

The product distribution from the experiments where an excess of NH_3 ensures fast deprotonation of the oxonium and the arenium ions, reducing their secondary isomerization, is believed to reflect accurately the relative abundances of the charged intermediates formed in the kinetically significant step of the alkylation, and underlines the bias in favour of the attack to oxygen.

It is worth noting the high (*ca.* 5) value of the apparent k(PhOH)/k(PhMe) ratio, especially significant in view of the generally low substrate selectivity of exothermic gas-phase substitutions, *e.g.* k(*m*-xylene)/k(PhMe) = 1·8 in the gas-phase t-butylation.

The remarkable selectivity of the t-$C_4H_9^+$ attack on oxygen is supported by the results obtained in the alkylation of anisole. In fact, the kinetically predominant attack of the gaseous electrophile on oxygen accounts for the higher overall reactivity of phenol with respect to anisole, despite the comparable reactivity of the aromatic ring in both substrates. The difference arises from the fact that, unlike (I), the oxonium ion (IV) cannot collapse directly into isolable products. Consequently, unless the reaction environment allows the occurrence of efficient isomerization of (IV) into (V) or (VI), which apparently is not the case in neopentane gas at 720 Torr, formation of t-butylated anisoles depends on the direct attack to the ring. Thus, the relatively low ($\leqslant$ 1·9) k(PhOMe)/k(PhMe) ratio measured at 720 Torr sets an upper limit to the rate of direct ring alkylation, which appears considerably slower than *O*-alkylation.

Despite their preliminary nature, the present results provide additional information on other mechanistically interesting features, especially in connection with the positional selectivity of the unsolvated electrophile. However, discussion of this problem requires more detailed data, in particular direct kinetic evidence on the fate of the methyl-t-butyl-phenyloxonium ion (IV), and its alkylating ability.

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