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An Alternative Route to Electrophilic Substitution. 2. Aromatic Alkylation in the Ion Neutral Complexes Formed upon Addition of Gaseous Arenium Ions to Olefins[1]

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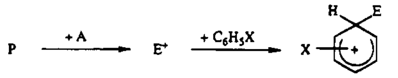
Abstract: The joint application of mass spectrometric and radiolytic techniques has allowed demonstration of an alternative route to electrophilic aromatic substitution operative in the gas phase, where the Wheland intermediate is formed within the ion−neutral complex (INC) formed upon addition of an arenium ion to an olefin. Experiments involving several representative pairs of arenium ions $XC_6H_6^+$ (X = H, CH_3, CF_3) and olefins (C_3H_6, $i$$C_4H_8$, $c$$C_5H_8$) have provided conclusive evidence for the operation of the above reaction sequence and hence for the occurrence of intracomplex alkylation. The peculiar mechanistic features of the reaction fit a model that identifies the relative basicity of the arene and of the olefin associated in any given INC as the key kinetic factor. The model accounts for the seemingly paradoxical observation that the alkylated products from *less* activated substrates are formed at relatively *higher* rates and for the occurrence of consecutive alkylation steps, yielding polyalkylated products of the less activated substrates. The relevance of the work to the theory of the aromatic substitution as a new entry into the reaction manifold of Friedel−Crafts alkylation and to gas-phase ion chemistry, as an irrefutable demonstration of the kinetic role of INCs is briefly discussed.

Introduction

Electrophilic aromatic substitution proceeds in many cases according to the general reaction sequence

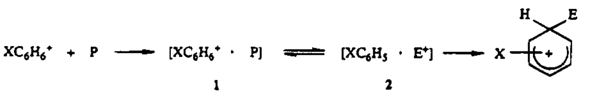


(1)

where P denotes a proelectrophile, namely a species devoid, per se, of electrophilic character, whose activation by the Brønsted or the Lewis acid A generates the electrophilic reagent E^+. Among the numerous examples of proelectrophiles one can cite alkenes, alkyl halides, alcohols, epoxides, acyl halides, nitriles, etc. in aromatic alkylation and acylation, hypohalous acids and their esters in halogenation, nitrous acid and its esters in nitrosation, nitric acid and alkyl and acyl nitrates in nitration, hydrazoic acid and organic azides in amination, hydrogen peroxide and alkyl peroxides in hydroxylation, etc.[2]

In conventional reactions, formation of the E^+ electrophile and its attack on the C_6H_5X substrate are temporally and spatially separated events, in that aromatic substitution involves the encounter of the substrate with the electrophile formed in a preliminary step and dispersed in the reaction medium or on a solid catalyst.

An alternative route is conceivable, whereby the electrophilic substitution occurs within the complex formed upon addition of an arenium ion to the proelectrophile, e.g.



(2)

This sequence embodies a distinct reaction pathway, with special kinetic and mechanistic features, only if aromatic substitution does actually occur within the complex, without separation of the reagents. If, on the contrary, E^+ escapes into the medium and reacts with the aromatic substrate at some later stage, the whole sequence 2 reduces to a conventional substitution 1 whose only peculiarity is that the acid used to activate the proelectrophile is an arenium ion.

The concept outlined in eq 2 is not new, e.g., it has long been envisaged by Olah in the specific case of Friedel−Crafts alkylation by olefins,[3] but mechanistic discrimination from the conventional reaction pathway 1 proved extremely difficult in solution, which has prevented further developments.

As part of our continuing interest in the reactivity of gaseous cations,[4,5] we have undertaken a systematic study of electrophilic aromatic substitution occurring within the gaseous ion−neutral complexes (INC) formed upon addition of arenium ions to a variety of proelectrophiles. The investigation, performed with a combination of mass spectrometric and radiolytic techniques, was prompted, first, by an interest in demonstrating an alternative entry into the reaction manifold of aromatic substitution exploiting the unique features of gas-phase ionic processes. Second, investigation of the kinetic and mechanistic features peculiar to reaction sequence 2 appeared highly promising, in view of the extremely short lifetime of the E^+ reagent prior to capture by the aromatic substrate contained in the same INC, e.g., isomerization of highly unstable cations could in principle be reduced or suppressed. Third, it was hoped that the results might provide additional and more conclusive evidence on the kinetic and mechanistic role of ICNs, currently the focus of

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active theoretical and experimental interest in gas-phase ion chemistry.[6-11] Among the different classes of electrophilic substitution investigated, the one to be discussed here is aromatic alkylation *via* sequence 2, where alkenes and cycloalkenes are used as proelectrophiles.

Experimental Section

Materials. The gases were research products obtained from Matheson Gas Products Inc. or Sigma-Aldrich srl with a stated purity exceeding 99.95 mol % (Ar, O_2, CH_4, CF_4) and 99 mol % (C_3H_6, iC_4H_8, $(CH_3)_2O$). CH_3F, purchased from Fluorochem Ltd. with a stated purity of 99 mol %, contained $(CH_3)_2O$, ca. 0.15 mol %, and traces of acetone, as shown by analyses performed by GC and GC/MS. C_6D_6, with a stated isotopic purity in excess of 99.96 atom %, was obtained from Sigma-Aldrich srl. All other chemicals were research grade products from commercial sources or were prepared according to standard procedures, e.g., in the case of isomeric cymenes, isopropyltrifluorotoluenes, *tert*-butyltoluenes, and cyclopentyltoluenes.

Instruments. The FT-ICR mass spectra were recorded using a Bruker Spectrospin Apex TM 47e instrument, equipped with an external ion source, two computer-controlled pulsed valves, and a XMass data system. The radiolytic products were analyzed by GC/MS using a HP 5890 GC coupled to a HP 5970 B mass-selective detector, from Hewlett-Packard Co., and a VG Micromass TRIO 1 benchtop GC/MS. In addition, a HP 5890 GC, equipped with a FID, was used for the quantitative analysis of the products.

Radiolytic Experiments. The gaseous samples were prepared according to standard procedures, using a greaseless vacuum line, in sealed 135-mL Pyrex vessels. The irradiations were performed in a 220 Gammacell from Nuclear Canada Ltd. equipped with a thermostatic device designed to maintain the sample to within ±1 °C from any desired temperature in the range from 40° to 150 °C. The irradiation time was 2 h, the total dose 1×10^4 Gy. Following the irradiation, the vessel was cooled to 77 K, and its contents dissolved into CH_3OH, carefully washing the inner walls, and performing repeated freeze–thaw cycles. The nature, the yields, the D content, and its intramolecular distribution in the aromatic products were determined by GC, using the internal-standard method, and by GC/MS, making use, when required, of specifically labeled reference standards. The column used was a 50-m long, 0.2-mm i.d. fused-silica capillary column, coated with a 0.5 μm layer of cross-linked methylsilicone phase (PONA column from HP) operated in the temperature range from 70° to 220 °C.

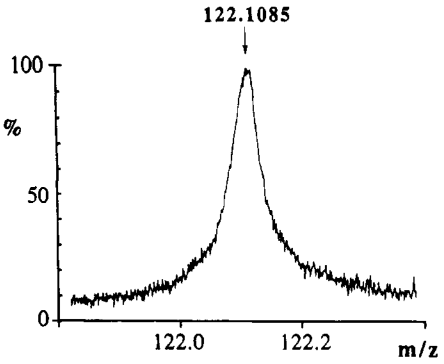

Figure 1. The $C_9H_{12}D^+$ peak, calculated *m/z* =122.10800, from the addition of $C_6H_6D^+$ to C_3H_6.

Table 1. Relevant Thermochemical Data

reaction	$\Delta H°$, kcal mol^{-1}
(3) $COH^+ + C_6H_6 = CO + (C_6H_7)^+$	-39.4,[a] −38.1[b]
(4) $(CH_3)_2F^+ + C_3H_6 = CH_3F + sC_4H_9^+$	−33.0[c]
(5) $(CH_3)_2F^+ + C_6H_6 = CH_3F + (CH_3C_6H_6)^+$	−43.0,[a,d] −40.5[b,d]
(7) $sC_4H_9^+ + C_6H_6 = (sC_4H_9C_6H_6)^+$	−33.3[d,e]
(9) $(CH_3C_6H_6)^+ + (CH_3)_2O = CH_3C_6H_5 + (CH_3)_2OH^+$	−2.3[a]
(10) $(CH_3C_6H_6)^+ + C_3H_6 = (CH_3C_6H_5\,iC_3H_7)^+$	−28.3[f]
(12) $CH_5^+ + C_3H_6 = CH_4 + iC_3H_7^+$	−47.9,[a] −48.2[b]
(13) $CH_5^+ + C_6H_6 = CH_4 + C_6H_7^+$	−49.7,[a] −50.0[b]
(15,25) $iC_3H_7^+ + C_6H_6 = (iC_3H_7C_6H_6)^+$	−35.7[a,d]
(18) $C_6H_7^+ + C_3H_6 = (iC_3H_7C_6H_6)^+$	−33.9,[a,d] −34.1[b,d]
(20) $CF_3^+ + C_6H_6 = (CF_3C_6H_6)^+$	58.7[d,g]
(22) $(CF_3C_6H_6)^+ + C_3H_6 = (CF_3C_6H_5\,iC_3H_7)^+$	ca. −85[h]
(27) $(CH_3C_6H_6)^+ + iC_4H_8 = (CH_3C_6H_5\,tC_4H_9)^+$	−24.3[a,d,i]

[a] According to the NIST database, ref 12. [b] According to the revised PA scale of ref 13. [c] From the heat of formation of $(CH_3)_2F^+$, ref 14 and 15, and of $sC_4H_9^+$, ref 12. [d] Referred to formation of the most stable protomer. [e] Estimated from the data of ref 12. [f] Referred to formation of protonated *p*-cymene, taking the PA of the latter equal to that of cumene, ref 12. [g] From the theoretically calculated PA of $CF_3C_6H_5$ see ref 16. [h] From the heat of formation of *p*-$CF_3C_6H_4iC_3H_7$, and its PA, estimated by the group method. [i] Referred to formation of protonated *p*-*tert*-butyltoluene, taking the PA of the latter equal to that of *tert*-butylbenzene, ref 12.

Results

Mass Spectrometric Results. The CH_4/CI spectra of gaseous mixtures containing C_6H_6 and olefins, recorded at 150 °C at pressures from 0.1 to 0.5 Torr, display peaks whose *m/z* ratios are those expected for the corresponding arenium ions, e.g., the $C_6H_6iC_3H_7^+$ ion in the CH_4/CI of benzene/propene mixtures. Whereas these experiments demonstrate the occurrence of gas-phase isopropylation, they give no information as to whether, and to what an extent, alkylation occurs *via* sequence 2. ICR spectrometry, with its unique ability to establish parent–daughter relationships in consecutive ion–molecule reactions, is the technique of choice to discriminate among channels 1 and 2. Unfortunately, the charged products from exothermic addition reactions, such as the final step of sequence 2, are bound to undergo back dissociation in the low-pressure range (10^{-8}–10^{-7} Torr) typical of FT-ICR experiments, which generally prevents detection of the alkylated aromatic adducts. E.g., preliminary FT-ICR experiments were performed, where $C_6H_6D^+$ ions, *m/z* = 80, obtained in the external source of the spectrometer by CO-D_2/CI of $^{12}C_6$-C_6H_6 according to the highly exothermic (Table 1) process, were driven into the resonance

$$DCO^+ + C_6H_6 \rightarrow CO + C_6H_6D^+ \qquad (3)$$

cell, isolated by selective-ejection techniques, and allowed to react with C_3H_6 contained in the cell at a low stationary pressure (1−5) × 10^{-8} Torr. As anticipated, no $C_9H_{12}D^+$ ions from sequence 2 were detected, owing to their complete back dissociation. However, by using a pulsed valve, one can obtain, albeit for a short time (<5 ms), C_3H_6 pressures up to 5 × 10^{-5} Torr, which allows collisional stabilization of a fraction of the excited $C_9H_{12}D^+$ ions, and hence their positive identification by accurate mass measurement (Figure 1). Despite their low relative intensity (<5%), detection of the alkylated adducts is significant, since they can only arise *via* intracomplex alkylation, according to the sequence

$$C_6H_6D^+ + C_3H_6 \rightarrow [INC] \rightarrow C_9H_{12}D^+ \qquad (2a)$$

In fact, no C_6H_6 was introduced into the reaction cell,[17] which excludes the role of any free isopropyl ion in the formation of the observed $C_9H_{12}D^+$ ions.

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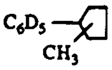
Table 2. Radiolytic Alkylation

T (K)	system composition (Torr)[a]		products yields[b] G(+M) × 100				products ratios
				Isopropylation			
	C_3H_6[c]	$(CH_3)_2O$	$C_6D_5CH_3$	$C_6D_5iC_3H_7$	$C_6D_5sC_4H_9$	$CH_3C_6D_4iC_3H_6D$	$CH_3C_6D_4iC_3H_6D:C_6D_5CH_3$
315	5.0	1.0	14.0	6.4	6.7	0.018[d]	0.001
353	5.0	1.0	24.9	1.0	6.6	0.17	0.007
353	9.0	1.0	38.1	0.4	7.2	0.50	0.013
353	20.0	1.0	12.4	9.8	6.8	0.26	0.021
393	5.0	1.0	31.8	1.3	9.8	1.0	0.031
408	5.0	1.0	19.3	0.8	10.8	0.7	0.036
	C_3H_6[e]	$(C_2H_5)_3N$	$C_6D_5iC_3H_7$	$C_6HD_4iC_3H_6D$	$C_6Y_4(iC_3Y_7)_2$[f]	$C_6Y_3(iC_3Y_7)_3$	
315	10.0	0.2	11.5	24.4	2.5[f]	n.d.	
353	10.0	0.2	13.9	21.8	3.2	0.03	
393	10.0	0.2	15.0	19.8	4.2	n.d.	
	C_3H_6[g]	$(CH_3)_2O$	$C_6D_5CF_3$	$C_6D_5iC_3H_6Y$[h]	$CF_3C_6D_4iC_3H_6D$[i]		$CF_3C_6D_4iC_3H_6D:C_6D_5CF_3$
315	10.0	1.1	9.0	11.0	1.2		0.13
	315	10.0	1.1	8.0	6.3	0.9	0.11
				tert-Butylation			
	iC_4H_8[j]	$(CH_3)_2O$	$C_6D_5CH_3$	$[CH_3C_6D_4tC_4H_8D]$			$CH_3C_6D_4tC_4H_6D:C_6D_5CH_3$
315	10.0	1.0	12.8	0.26 (m = 27%, p = 73%)			0.026
353	10.0	1.0	29.8	0.15 (m = 28%, p = 72%)			0.014
393	10.0	1.0	29.8	0.16 (m = 40%, p = 60%)			0.005
				Cyclopentylation			
	$c\text{-}C_5H_{10}$[k]	$(CH_3)_2O$	$C_6D_5CH_3$	$C_6D_5cCH_5H_9$		$CH_3C_6D_4cC_5H_8D$	$CH_3C_3D_4cC_5H_8D:C_6D_5CH_3$
315	10.0	1.0	11.7	1.2	0.88	0.67[l]	0.06
353	10.0	1.0	17.3	1.0	0.50	1.5	0.09
353	10.0	5.1	12.5	0.40	0.15	0.059	0.05
353	10.0	10.1	12.3	0.17	0.10	0.033	0.03
393	10.0	1.0	13.2	0.40	0.16	0.014	0.11

[a] All systems contained 720 Torr of the bulk gas and O_2, 10 Torr. [b] Standard deviation of the yields ±10%, increasing to ±20% for $G_{(+M)}$ values $<10^{-3}$. [c] Bulk gas CH_3F, C_6D_6 1.5 Torr. [d] Isomeric composition of cymenes, o = 50%, m = p = 25%. [e] Bulk gas CH_4, C_6D_6 3 Torr. [f] Isomeric composition of di*i*propylbenzenes, o = 47%, m = 22%, p = 31%; Y = H, D. [g] Bulk gas CF_4, C_6D_6 2.4 Torr. [h] Y = H, D in the approximate 4:1 ratio. [i] m = 75%, p = 25%, also formed $CF_3C_6D_3$ $(iC_3H_6D)_2$ and $CF_3C_6D_2$ $(iC_3H_6D)_3$. [j] Bulk gas CH_3F, C_6D_6 3.0 Torr. [k] Bulk gas CH_3F, C_6D_6 1.2 Torr. [l] Isomeric composition of cyclopentyltoluenes o = 40%, m = 29%, p = 31%.

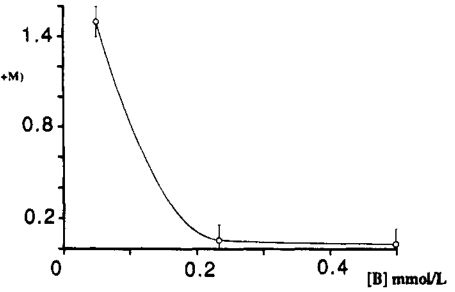


Figure 2. Depression of the radiolytic yields of aromatic products from gas-phase cyclopentylation upon addition of increasing amounts of $(C_2H_5)_3N$.

In summary, the results show that charged products whose *m*/*z* ratio corresponds to that expected for alkylated arenium ions are formed upon addition of benzenium ions to propene, in a process that occurs without separation of the reactants after their encounter. The results are consistent with, but fall short of proving, operation of sequence 2, in that the lack of structural discrimination of FT-ICR spectrometry does not allow for the exclusion of the possibility that the $C_9H_{12}D^+$ ions observed are noncovalent complexes, rather than protonated cumene.

Radiolytic Alkylation. Methodology. This technique, whose principles, experimental details, and applications have been reviewed,[4] is based on the γ irradiation of a gaseous system whose bulk component gives upon ionization the charged reagent of interest, *via* a well-defined sequence of reactions. Following complete collisional thermalization, the ion interacts with the aromatic substrate(s), giving charged intermediates whose deprotonation yields neutral end products, analyzed by GC, GC/MS, or NMR. The radicals cogenerated in the radiolysis together with the charged species are trapped by an efficient scavenger (O_2) present at a relatively high concentration in the gas. In any case, the ionic origin of the products of interest is independently confirmed by the depression, and eventually the suppression, of their yields caused by increasing concentrations of interceptors, e.g., bases, that trap the charged species (Figure 2). Furthermore, independent evidence for the postulated ionic reagents and intermediates is obtained from the mass spectrometric study of the same system, and, finally, the very nature of the products, e.g., the alkylated arenes relevant to this work, often indicates their ionic origin.

The results from the study of the reactions investigated are summarized in Table 2, where the yields of the products are expressed by their $G_{(+M)}$ values, namely the number of molecules formed per 100 eV absorbed.

Isopropylation. Three primary charged reagents have been used, namely $(CH_3)_2F^+$, $C_nH_5^+$ ($n = 1, 2$), and CF_3^+, obtained from the irradiation of CH_3F, CH_4, and CF_4, respectively. $(CH_3)_2F^+$ is the major stable ion formed, together with traces of CH_3FH^+, upon ionization of gaseous CH_3F, according to fast, consecutive ion−molecule reactions firmly established by mass spectrometric and radiolytic studies.[18−22] The $(CH_3)_2F^+$ ions react with C_3H_6 and C_6D_6 according to the sequence of ion−molecule reactions illustrated by the simplified scheme A of Chart 1. The paramount result is the formation of $CH_3C_6D_4$-

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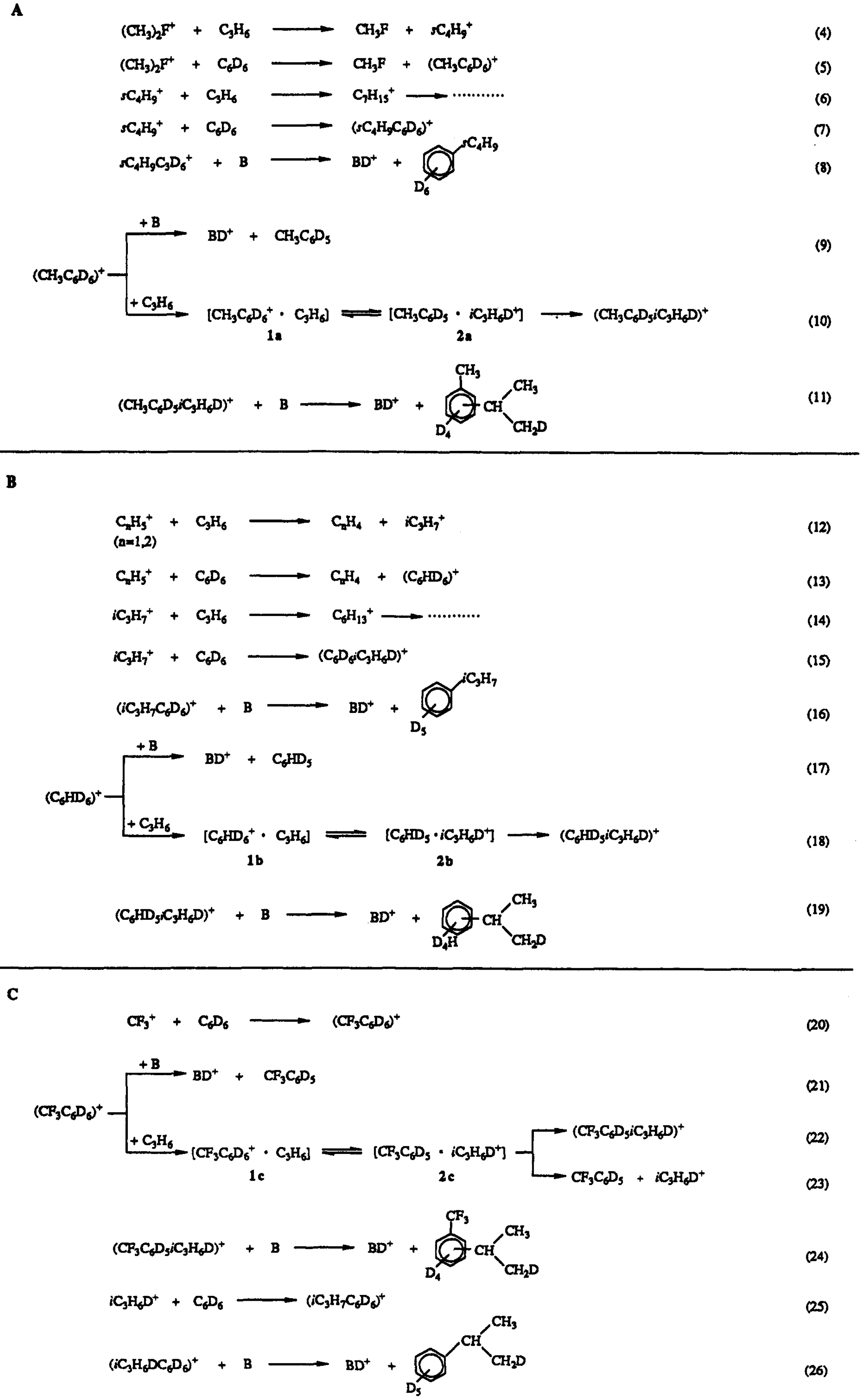
Chart 1


A
$(CH_3)_2F^+ + C_3H_6 \longrightarrow CH_3F + sC_4H_9^+$ (4)
$(CH_3)_2F^+ + C_6D_6 \longrightarrow CH_3F + (CH_3C_6D_6)^+$ (5)
$sC_4H_9^+ + C_3H_6 \longrightarrow C_7H_{15}^+ \longrightarrow \cdots\cdots$ (6)
$sC_4H_9^+ + C_6D_6 \longrightarrow (sC_4H_9C_6D_6)^+$ (7)
$sC_4H_9C_3D_6^+ + B \longrightarrow BD^+ +$ (8)
sC_4H_9
D_6
$(CH_3C_6D_6)^+ \xrightarrow{+B} BD^+ + CH_3C_6D_5$ (9)
$(CH_3C_6D_6)^+ \xrightarrow{+C_3H_6} [CH_3C_6D_6^+ \cdot C_3H_6] \rightleftharpoons [CH_3C_6D_5 \cdot iC_3H_6D^+] \longrightarrow (CH_3C_6D_5iC_3H_6D)^+$ (10)
1a
2a
$(CH_3C_6D_5iC_3H_6D)^+ + B \longrightarrow BD^+ +$ (11)
CH_3
CH
CH_3
CH_2D
D_4
B
$C_nH_5^+ + C_3H_6 \longrightarrow C_nH_4 + iC_3H_7^+$ (12)
(n=1,2)
$C_nH_5^+ + C_6D_6 \longrightarrow C_nH_4 + (C_6HD_6)^+$ (13)
$iC_3H_7^+ + C_3H_6 \longrightarrow C_6H_{13}^+ \longrightarrow \cdots\cdots$ (14)
$iC_3H_7^+ + C_6D_6 \longrightarrow (C_6D_6iC_3H_6D)^+$ (15)
$(iC_3H_7C_6D_6)^+ + B \longrightarrow BD^+ +$ (16)
iC_3H_7
D_5
$(C_6HD_6)^+ \xrightarrow{+B} BD^+ + C_6HD_5$ (17)
$(C_6HD_6)^+ \xrightarrow{+C_3H_6} [C_6HD_6^+ \cdot C_3H_6] \rightleftharpoons [C_6HD_5 \cdot iC_3H_6D^+] \longrightarrow (C_6HD_5iC_3H_6D)^+$ (18)
1b
2b
$(C_6HD_5iC_3H_6D)^+ + B \longrightarrow BD^+ +$ (19)
CH
CH_3
CH_2D
D_4H
C
$CF_3^+ + C_6D_6 \longrightarrow (CF_3C_6D_6)^+$ (20)
$(CF_3C_6D_6)^+ \xrightarrow{+B} BD^+ + CF_3C_6D_5$ (21)
$(CF_3C_6D_6)^+ \xrightarrow{+C_3H_6} [CF_3C_6D_6^+ \cdot C_3H_6] \rightleftharpoons [CF_3C_6D_5 \cdot iC_3H_6D^+] \longrightarrow (CF_3C_6D_5iC_3H_6D)^+$ (22)
$\longrightarrow CF_3C_6D_5 + iC_3H_6D^+$ (23)
1c
2c
$(CF_3C_6D_5iC_3H_6D)^+ + B \longrightarrow BD^+ +$ (24)
CF_3
CH
CH_3
CH_2D
D_4
$iC_3H_6D^+ + C_6D_6 \longrightarrow (iC_3H_7C_6D_6)^+$ (25)
$(iC_3H_6DC_6D_6)^+ + B \longrightarrow BD^+ +$ (26)
CH
CH_3
CH_2D
D_5

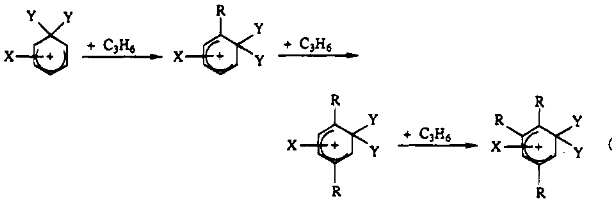
$CH(CH_3)CH_2D$ isomeric cymenes, whose nature, isotopic distribution, and yields have been established by GC and GC/MS. Their formation can only occur *via* reactions 10 and 11, since alkylation of toluene by free $iC_3H_6D^+$ ions is ruled out, under the experimental conditions chosen, by the fact that no toluene is present in the gas, except for the very small amounts formed during the radiolysis e.g., *via* reactions 5 and 9. Given the enormous excess of C_3H_6 and C_6D_6 as well as the indiscriminate reactivity of free *i*propyl cation,[23] any deuterated cymenes formed from free $iC_3H_6D^+$ ions would be orders of magnitude below the detection limit. Accordingly, formation of $CH_3C_6D_4iC_3H_6D$ isomers provides compelling evidence for the operation of intracomplex alkylation 2. According to scheme A of Chart 1, the efficiency of the process depends on the competition between deprotonation 9 and the alkylation sequence 10, and hence the ratio R between the yield of $CH_3C_6D_4iC_3H_6D$ and of $CH_3C_6D_5$ obeys the relation $R = k_{10}[C_3H_6]/k_9[B]$. For a fixed value of [B], R should linearly increase with $[C_3H_6]$, an expectation borne out by the results of competition experiments (Figure 3).

Remarkably, R undergoes a sharp increase with the temperature, reflecting the corresponding increase of the k_{10}/k_9 ratio illustrated in Figure 4. Since the exothermic proton transfer 9 to an unhindered n-type base is expected to be a fast, weakly temperature-dependent process,[24] the trend is most likely traced to the increase of k_{10} with the temperature. Interestingly, the isomeric composition of the cymenes from reactions 10 and 11 corresponds, within experimental errors, to that observed in the direct alkylation of toluene by free $iC_3H_7^+$ ions [23] (*vide infra*).

The results show that the $iC_3H_6D^+$ ions quantitatively react with $CH_3C_6D_5$ within complex **2a** without escaping into the gaseous medium, where they would be trapped by C_6D_6 yielding $iC_3H_6DC_6D_5$, which has not been detected among the products.

Formation of *sec*-$C_4H_9C_6D_5$ is readily accommodated by the consecutive reactions 4, 7, and 8 of scheme A, whereas $iC_3H_7C_6D_5$ is produced from the alkylation of C_6D_6 by free, unlabeled isopropyl ions from the protonation of propene by radiolytically formed Brønsted acids such as CH_3FH^+, H_3O^+, etc.

A different approach has been based on the use of CH_5^+ and $C_2H_5^+$, the major ions formed with a combined $G_{(+M)}$ value of ca. 3 in neat irradiated CH_4.[25] Their interaction with C_3H_6 and C_6D_6 promotes the ionic reaction pattern illustrated, in a simplified form, in scheme B of Chart 1. The salient result is the formation of cumene of the isotopic composition $C_6HD_4CH(CH_3)CH_2D$, demonstrated by its EI mass spectrum that displays equally intense (M − 15) and (M − 16) peaks, arising from the loss of CH_2Y (Y = H,D), according to a fragmentation pattern typical of isopropylated arenes. Formation of $C_6HD_4CH(CH_3)CH_2D$ can only be traced to deprotonation of an arenium ion formed within the complex **2b**, since any free $iC_3H_6D^+$ ions would be trapped by C_6D_6, yielding instead $C_6D_5CH(CH_3)CH_2D$ as the final product. The failure to detect the latter indicates that no $iC_3H_6D^+$ ions escape from **2b**. The $iC_3H_7C_6D_5$ cumene, formed in significant yields, arises from the attack on C_6D_6 of the $iC_3H_7^+$ ions formed upon protonation of C_3H_6 by $C_nH_5^+$. The efficiency of the alkylation 18 is appreciably higher than of the corresponding process 10, and, in addition, it is nearly independent of the temperature. Another interesting feature is the formation of di-, and even triisopropylbenzenes, pointing to operation of consecutive alkylation steps in the complexes formed upon addition of increasingly substituted arenium ions to propene.



(18a)

(X=H, CF_3; Y=H,D ; R=iC_3H_7)

The third reagent used, CF_3^+, is the major cation formed upon ionization of CF_4 and is unreactive toward the parent molecule.[4] Irradiation of C_3H_6 and C_6D_6 highly diluted in CF_4 gas promotes the ionic reactions illustrated in the simplified scheme C of Chart 1. Occurrence of the alkylation within complex **2c** is demonstrated by formation of $CF_3C_6D_4iC_3H_6D$ isomers, a process which can only occur *via* sequence 22. However, at variance with the alkylation reactions previously discussed, there is evidence that a fraction of the $iC_3H_6D^+$ ions formed within complex **2c** fails to react with $CF_3C_6D_5$, a strongly deactivated substrate, and escapes into the gaseous medium, where the ions are trapped by C_6D_6, giving $C_6D_5iC_3H_6D$, detected in significant yields among the products.

***tert*-Butylation.** Irradiation of gaseous systems containing iC_4H_8 and C_6D_6 highly diluted in CH_3F promotes a sequence of ionic reactions analogous to those illustrated in the scheme A of Chart 1. Isolation of isomeric $CH_3C_6D_4tC_4H_8D$ *tert*-butyltoluenes among the products indicates operation of the alkylation pathway

$$(CH_3C_6D_6)^+ + iC_4H_8 \rightarrow \underset{\mathbf{1d}}{[(CH_3C_6D_6)^+ \cdot iC_4H_8]} \rightleftarrows \underset{\mathbf{2d}}{[CH_3C_6D_5 \cdot tC_4H_8D^+]} \rightarrow (CH_3C_6D_5tC_4H_8D)^+ \quad (27)$$

$$(CH_3C_6D_5tC_4H_8D)^+ + B \rightarrow BD^+ + CH_3C_6D_4tC_4H_8D \quad (28)$$

As in isopropylation, the isotopic composition of *tert*-butyltoluenes, in particular the presence of a D atom in a methyl group of the *tert*-butyl substituent, is only consistent with intracomplex alkylation. The efficiency of the process, expressed by the k_{27}/k_9 ratio deduced from the product ratio R, decreases at higher temperatures (Figure 5), whereas the extent

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(15) The data of ref 14 have been adjusted to the scale revised by the following: Glukhovtsev, M. N.; Szulejko, J. E.; McMahon, T. B.; Gauld, J. W.; Scott, A. P.; Smith, B. J.; Pross, A.; Radom, L. *J. Phys. Chem.* **1994**, *98*, 13099.

(16) No published values of the PA of $C_6H_5CF_3$ are available. We have used the PA = 166.4 kcal mol^{-1} obtained from a MINDO study: Karaman, R.; Huang, J.-T. L.; Fry, J. L. *J. Org. Chem.* **1991**, *56*, 188.

(17) Despite efficient differential pumping of the transfer system, traces of C_6H_6 actually leak from the external ion source into the cell, but its concentration is far too low to account for the $C_9H_{12}D^+$ ions observed, especially in view of the large (more than 50 000-fold) excess of C_3H_6.

(18) Herod, A. A.; Harrison, A. G.; McAskill, N. A. *Can. J. Chem.* **1971**, *49*, 2217.

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(20) McMahon, T. B.; Kebarle, P. *Can. J. Chem.* **1985**, *63*, 3160.

(21) Hollis, J.; Tedder, J. M.; Walker, G. S. *J. Chem. Soc., Perkin Trans. 2* **1991**, 1187.

(22) Speranza, M.; Pepe, N.; Cipollini, R. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1179.

(23) The lack of selectivity of free $iC_3H_7^+$ is reflected by a $k_{toluene}:k_{benzene}$ ratio of 1.0 ± 0.1 in C_3H_8 at 720 Torr at 37.5 °C, and by the isomeric composition of the cymenes formed: o = 48%, m = 28%, p = 24%, according to the following: Attinà, M.; Cacace, F.; Ciranni, G.; Giacomello, P. *J. Chem. Soc., Perkin Trans. 2* **1979**, 891.

(24) Su, T., Bowers, M. T. *Gas Phase Ion Chemistry*; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 1, p 84.

(25) Ausloos, P.; Lias, S. G.; Gorden, R., Jr. *J. Chem. Phys.* **1963**, *39*, 3341.

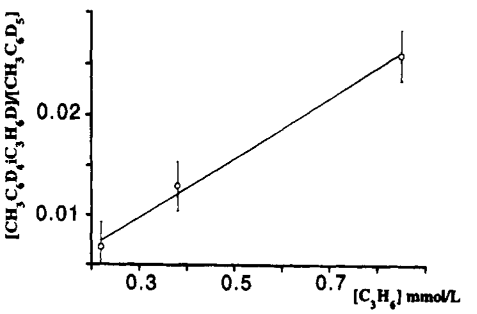


Figure 3. Increase of the relative efficiency of isopropylation with the concentrations of propene, see text.

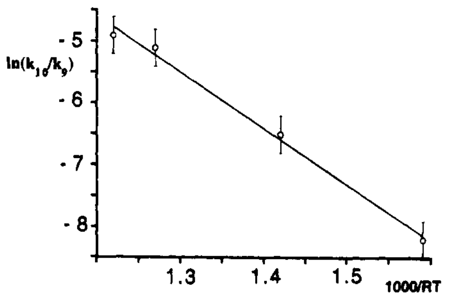


Figure 4. Temperature dependence of the k_{10}/k_9 ratio, see text.

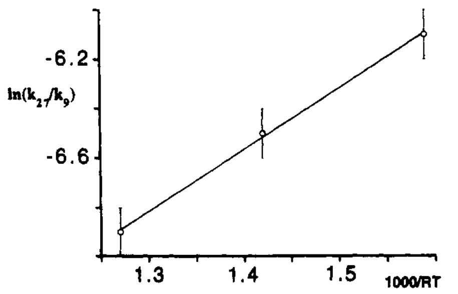
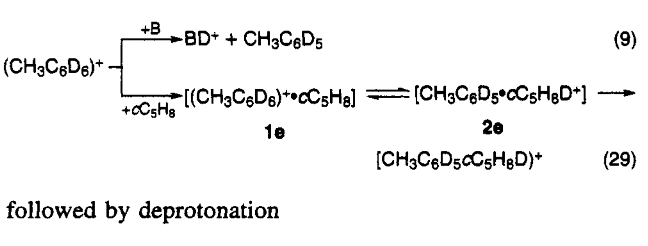


Figure 5. Temperature dependence of the k_{27}/k_9 ratio, see text.

of meta substitution increases, consistent with the trend prevailing in gas-phase *tert*-butylation of toluene by free $tC_4H_9^+$ ions.[26,27]

Cyclopentylation. Irradiation of cC_5H_8 and C_6D_6 in excess CH_3F promotes aromatic cyclopentylation according to a reaction sequence analogous to that illustrated in scheme A of Chart 1, whose key steps are the competitive processes



followed by deprotonation

$$(CH_3C_6D_5cC_5H_8D)^+ + B \rightarrow BD^+ + CH_3C_6D_4cC_5H_8D \quad (30)$$

The presence of a D atom in the cyclopentane ring of isomeric cpentyltoluenes shows that the alkylation occurs within complex **2e**. At a given $[cC_5H_8]$ value, the rate of cyclopentylation linearly decreases with [B], as shown in Figure 6, consistent with the postulated competition between reactions 9 and 29. The efficiency of the intracomplex alkylation, at any fixed $[cC_5H_8]$:[B] ratio, is expressed by the $CH_3C_6D_4cC_5H_8D/CH_3C_6D_5$ product ratio and shows a weakly positive temperature dependence (Figure 7). Formation of $C_6D_5cC_5H_9$ is traced to alkylation of C_6D_6 by free, unlabeled $cC_5H_9^+$ ions from the protonation of cC_5H_8 by radiolytically formed Brønsted acids, such as CH_3FH^+, H_3O^+, etc. The other product identified, methylcyclopentylbenzene, arises from the alkylation of C_6D_6 by methylcyclopentyl cations formed upon methylation of cC_5H_8 by $(CH_3)_2F^+$ ions.

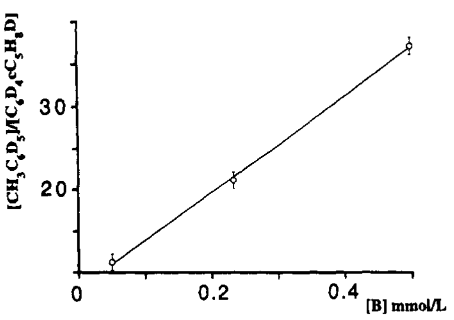


Figure 6. Dependence of the relative efficiency of cyclopentylation on the concentration of added $(CH_3)_2O$.

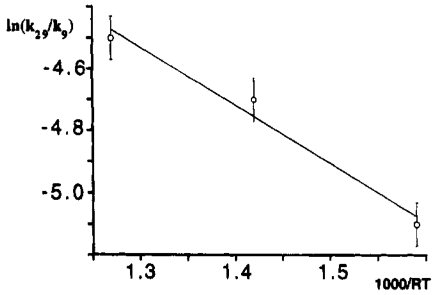


Figure 7. Temperature dependence of the k_{29}/k_9 ratio, see text.

Discussion

The results reported in the previous section demonstrate operation of intracomplex aromatic alkylation according to the sequence

$$(XC_6H_6)^+ + \text{olefin} \rightleftharpoons [(XC_6H_6)^+\cdot\text{olefin}] \rightleftharpoons [XC_6H_5\cdot R^+] \rightleftharpoons \sigma\ \text{complex} \quad (2)$$

outlining a peculiar, yet mechanistically informative reaction pattern, whose salient feature is the *higher* rate of the reactions yielding alkylated derivatives of *less* activated substrates. E.g., preliminary experiments have shown that ethylation by C_2H_4 occurs when $X = CF_3$, but not when $X = H$, or CH_3, and comparison between alkylation of $(CH_3C_6H_6)^+$ and of $(C_6H_7)^+$ by C_3H_6 shows that the latter process is faster and displays a weakly *negative* temperature dependence, suggestive of the lack of an activation energy. Furthermore, polyisopropylation by C_3H_6 occurs from $(CF_3C_6H_6)^+$ and $(C_6H_7)^+$ but not from $(CH_3C_6H_6)^+$, whereas no alkylation at all is observed from the interaction of (*i*durene) H^+ with propene. By contrast, no $iC_3H_6D^+$ ions escape from complexes **2a** and **2b** containing $CH_3C_6D_5$ and C_6HD_5 as the neutral ligands, whereas there is evidence for the $iC_3H_6D^+$ loss from complex **2c**, containing $CF_3C_6D_5$.

Such contrasting, and in some respects seemingly paradoxical, features can be rationalized taking into account the relative stability of complexes **1** and **2**, and the barrier for their interconversion, that depends on the balance between the basicities of the arene and of the olefin involved, whose proton affinities (PA) are reported for convenience in Table 3.

Let us consider first the pairs where $\Delta PA = PA\ (\text{arene}) - PA(\text{olefin})$ is large, say >20 kcal mol^{-1}, e.g., in the case of toluene *vs* ethylene or *i*durene *vs* propene. Despite the larger ion–molecule interaction energy and hence the higher stabilization expected for complexes **2** with respect to the corresponding

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(26) Cacace, F.; Ciranni, G. *J. Am. Chem. Soc.* **1986**, *108*, 887.

(27) Cacace, F.; Crestoni, M. E.; Fornarini, S. *J. Am. Chem. Soc.* **1992**, *114*, 6776 and references therein.

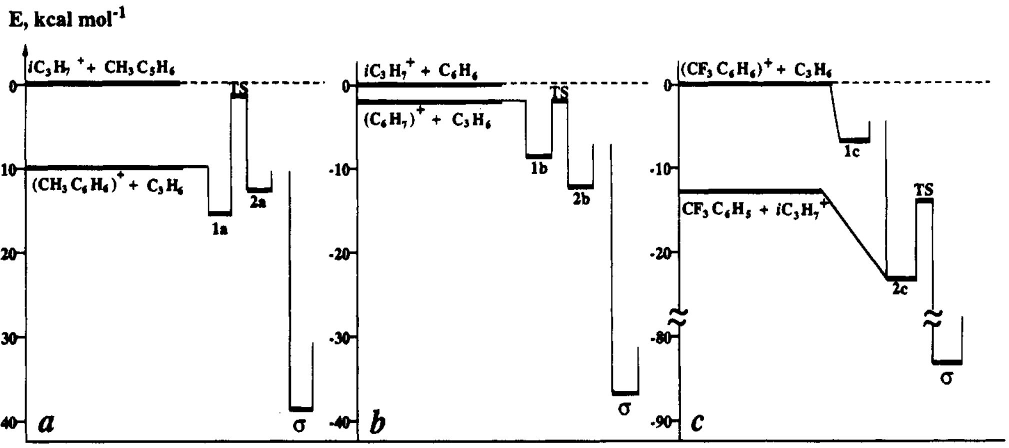

Figure 8. Schematic potential energy-reaction coordinate diagram for the reactions with propene of (a) toluenium ion, (b) benzenium ion, and (c) trifluoromethylbenzenium ion.

Table 3. Proton Affinity of Arenes and Olefins

base	PA, kcal mol^{-1}
C_6H_6	181.3,[a] 180.0[b]
$CH_3C_6H_5$	189.8,[a] 187.7[b]
$CF_3C_6H_5$	≥166.4[c]
C_2H_4	162.6[a,b]
C_3H_6	179.5,[a] 178.4[b]
iC_4H_8	195.9,[a] 191.7[b]
cC_5H_8	ca. 189[d]

[a] From ref 12. [b] From ref 13. [c] From ref 16. [d] Estimated value, taken equal to the PA of c-C_6H_{10}, ref 12.

complexes **1**,[28] the latter ones are much more stable in the case considered, which introduces a large endothermicity component into the barrier for **1** → **2** conversion, thus blocking the whole alkylation sequence 2.

Next we turn to pairs whose ΔPA is smaller, say 10 kcal mol^{-1}, as in the case of toluene *vs* propene, illustrated in the schematic energy diagram of Figure 8a. Apart from the heats of formation of the free reactants and of the σ complex, deduced from literature values,[12,13] the diagram should be regarded as qualitative, since the reported energies of complexes **1a** and **2a** are educated guesses that however are not inconsistent with theoretical estimates for related systems.[11] The stability gap due to the higher PA of toluene than of propene is assumed to be considerably reduced by the higher interaction energy in **2a** than in **1a**, making the **1a** → **2a** conversion only moderately endothermic. Under the additional assumption that the activation energy for the alkylation sequence 2 is associated to the **1a** → **2a** conversion step, the experimental value of 9.1 ± 1.0 kcal mol^{-1} from the Arrhenius plot of Figure 4 represents the ΔE_a difference between the barrier for the back dissociation of **1a** and for its conversion into **2a**, leading to a E_a value of ca. 14 kcal mol^{-1} for the latter process. Upon subtraction of the endothermicity term, the intrinsic barrier for D^+ transfer from the toluenium ion to propene in complex **1a** can be estimated of the order of 10 kcal mol^{-1}. Albeit largely approximate, this value is reasonably close to those derived from experimental and theoretical methods for related processes. The only available experimental E_a value for *thermal*, gas-phase $H^+(D^+)$ transfer between π-type centers, that refers to interannular exchange in protonated diphenylethane, amounts to 6.3 (8.0) kcal mol^{-1}.[29] Furthermore, according to AM 1 semiempirical calculations, the intrinsic barrier for the slightly *exothemic* **1b** → **2b** conversion *via* H^+ transfer amounts to 6 kcal mol^{-1}.[30]

The case where ΔPA ≃ 0 is aptly illustrated by the benzene/propene pair (Figure 8b). Owing to its larger interaction energy, complex **2b** is appreciably more stable than **1b**, and according to the Hammond postulate the intrinsic barrier for **1b** → **2b** conversion is expected to be somewhat lower than in the previously discussed case. This expectation is borne out, since the observed weakly *negative* temperature dependence points to a barrier height not exceeding that for dissociation of **1b**, estimated on the order of 6 kcal mol^{-1} according to the results of semiempirical and *ab initio* calculations.[11] The estimated E_a value agrees as well with the height of the barrier from the above mentioned AM 1 study.[30] Analogous considerations apply to the toluene/*c*pentene and toluene/*i*butene pairs, whose ΔPA is also small.

Finally, an example where the PA of the olefin considerably exceeds that of the aromatic molecule, namely ΔPA < 0, is offered by the $CF_3C_6H_5/C_3H_6$ pair (Figure 8c). Here complex **1c** can evolve into complex **2c** *via* an exothermic process, presumably characterized by a barrier whose height is expected to be very small, according to the Hammond postulate. The efficiency of the alkylation sequence 2 depends on the k_{22}/k_{23} ratio, affected in turn by the relative height of the barriers for the formation of the Wheland intermediate from **2c** and for dissociation of the complex. The observation of a weakly negative temperature dependence suggests that the two barriers are comparable, pointing to an appreciable activation energy for the formation of the σ complex. Such a finding, that sets $CF_3C_6H_5$ apart from C_6H_6 and $CH_3C_6H_5$, befits the strong deactivation of the substrate, whose low reactivity toward gaseous cations was previously reported.[31] The special features outlined in the energy diagram of Figure 8c provide a reasonable explanation for the observed loss of $iC_3H_6D^+$ ions from complex **2c**.

The above discussion is based on the implicit assumption that the alkylation occurs *via* a stepwise mechanism where proton transfer to the olefin and formation of the σ complex are two distinct, consecutive processes. However, a concerted mechanism is also conceivable, and actually it has been considered in a mass spectrometrics study of the fragmentation of protonated arenes.[32] It is difficult to devise a crucial mechanistic test capable of rigorously discriminating between the stepwise and the concerted mechanism. The best argument we can offer is based on a comparative study of the isomeric

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[28] According to semiempirical calculations, ref 11, the interaction energy of complex **2** exceeds that of complex **1** by ca. 8 kcal mol^{-1} for the *p*-xylene/propene pair.

[29] Cacace, F.; Crestoni, M. E.; Fornarini, S.; Kuck, D. *J. Am. Chem. Soc.* **1993**, *115*, 1024.

[30] Berthomieu, D.; Audier, H.; Denhez, J. P.; Monteiro, C.; Mourgues, P. *Org. Mass Spectrom.* **1991**, *26*, 271.

[31] Attinà, M.; Cacace, F.; Yañez, M. *J. Am. Chem. Soc.* **1987**, *109*, 5092.

[32] Denhez, J. P.; Audier, H. E.; Berthomieu, D. *Org. Mass Spectrom.* **1993**, *28*, 704.

composition of the cymenes from the reaction of toluenium ions with propene (Table 2) and from the alkylation of toluene by bona fide isopropyl ions from the radiolysis of C_3H_8 at 720 Torr, in a series of specifically designed control experiments performed as described in earlier reports.[33] Significantly, the positional selectivity of the two processes is the same, within experimental errors, over the temperature range from 42 to 80 °C. This observation speaks against the operation of a concerted mechanism, unless one is willing to assume that the latter is characterized by the same activation parameters of the stepwise mechanism, a position that would strongly detract from the relevance of a discrimination between the two pathways.

Polyalkylation. A distinctive feature of the intracomplex alkylation is the formation of polysubstituted derivatives, particularly of the less activated aromatic substrates. E.g., as reported in a previous section, di- and triisopropylated products of $CF_3C_6H_5$ are formed, whereas no polyisopropylated toluenes have been detected. Such a peculiar trend finds a reasonable explanation if one takes into account the relative basicity of the arenes and the olefins involved in the consecutive alkylation steps. In the case of toluene, the first alkylation step yields protonated cymenes, whose conjugate bases are stronger than toluene. This increases the ΔPA basicity gap between the arene and propene, making the reaction

$$[(CH_3C_6Y_5iC_3Y_7)^+\ C_3H_6] \underset{(Y = H, D)}{\not\rightarrow} [CH_3C_6Y_4iC_3Y_7{\cdot}C_3H_6Y^+] \tag{31}$$

more endothermic than reaction 10, and hence the second alkylation step much slower than the first one. The situation is different in the case of $CF_3C_6H_5$. The first alkylation step gives protonated isopropyltrifluoromethylbenzenes, whose conjugate bases are still weaker than propene. As a consequence, conversion of the complexes **1** formed upon addition to propene into the corresponding complexes **2** is still not endothermic, and the second alkylation step is likely to be as efficient as the first one, or even more efficient, owing to the higher activation of certain $CF_3C_6H_4iC_3H_7$ isomers than of $CF_3C_6H_5$, which favors conversion of the corresponding complexes **2** into Wheland intermediates.

Conclusion

By exploiting the unique features of the gaseous reaction environment we have demonstrated the operation and outlined the special mechanistic features of an alternative route to electrophilic aromatic substitution occurring within the complexes formed upon addition of arenium ions to olefins. The results of a systematic survey currently under way in this laboratory show that reaction (2) is quite general. Far from being restricted to the use of olefins as the proelectrophiles, nor, for that matter, to aromatic alkylation, the process has been found to encompass many classes of substitution reactions, including nitrosation, nitration, amination, silylation, germylation, etc. that will be examined in forthcoming papers.

The intracomplex reaction (2) provides a new entry into the manifold of electrophilic substitution, of considerable potential interest in view of the very short lifetime, well below 10^{-9} s, of the charged electrophile prior to its capture by the aromatic molecule contained in the *same* ion–molecule complex, and hence having a very high local concentration. This might widen the scope of aromatic substitution to unstable electrophiles that in conventional bimolecular reactions undergo rearrangement or dissociation well before interacting with the aromatic substrate.

Finally, the present results are relevant to gas-phase ion chemistry, as a direct demonstration of a reaction occurring within a bona fide ion–neutral complex. The mechanistic role of INCs has long been postulated in mass spectrometry,[6–11] based however on indirect evidence related to the fragmentation pattern of excited species from the ionization of a parent molecule where the putative components of the complex were covalently bound. In a specific case of alkylarenium ions, the lack of irrefutable experimental evidence has forced recourse to theoretical approaches,[11,30] whose results, incidentally, despite the severe limitations imposed by the complexity of the system, do not appear inconsistent with the experimental evidence from this work.

By contrast, the approach outlined in this report provides positive evidence for the occurrence of electrophilic aromatic substitution within ion–molecule complexes *prepared by assembling their initially separate components*, exactly as in condensed-phase coordination chemistry. Furthermore, the complexes are thermally equilibrated with the dense gaseous environment, which allows meaningful definition of the reaction temperature, and confers generality to the results, making them amenable to the standard kinetic treatment universally used in solution chemistry.

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[33] Attinà, M; Giacomello, P. *J. Am. Chem. Soc.* **1979**, *101*, 6040.