

## Isomeric Alkyl Cation/Arene Complexes in the Gas Phase

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**Abstract:** The kinetics and the stereochemistry of the protonation-induced unimolecular isomerization of (*S*)-(+)-1-D<sub>1</sub>-3-(*p*-tolyl)butane have been investigated in the gas phase in the 100–160 °C range. The process leads to the almost exclusive formation of the relevant *meta* isomer with complete racemization and partial 1,2-H shift in the migrating *sec*-butyl group. These results, together with the relevant activation

parameters, point to the occurrence of low-energy, tightly bound isomeric *sec*-butyl cation/toluene complexes of defined structure and stability along the isomerization coordinate. The existence

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and the  $\eta^1$ -type structure of these low-energy intermediate species are confirmed by ab initio calculations on closely related systems at the MP2(full)/6-311++G\*\*//HF/6-31+G\*\* level of theory. Their role in the relevant energy surface clearly emerges from the comparison of the present results with those concerning *sec*-butylation of toluene carried out under comparable experimental conditions.

## Introduction

Noncovalent ion-neutral complexes (INC), first postulated in the study of bimolecular reactions, are widely recognized as intermediates in unimolecular isomerization and fragmentation of excited ions.<sup>[1–3]</sup> Their occurrence in electrophilic aromatic substitutions is nowadays supported by a variety of refined theoretical, spectroscopic, and mass spectrometric techniques, which provided precious information on their lifetime.<sup>[4–7]</sup> However, other INC key features, such as the mutual orientation of their components and the nature of the forces holding them together, usually escape precise determination because of intrinsic limitations of the available experimental methodologies.<sup>[8]</sup> This lack of information is particularly unsatisfactory since, in principle, the nature and the dynamics of the INC components may control their evolution to products and, thus, determine the selectivity of

the process. This paper is aimed at providing a novel interpretation of the factors governing the positional selectivity in a representative gas-phase electrophilic aromatic substitution, that is the *sec*-butylation of toluene, based on a careful investigation of the nature and the dynamics of the INC involved.

Some insights into the nature and the relative stability of the noncovalent INC structures involved in these reactions were given by Audier and co-workers who calculated the potential energy profiles (PES) of several arene alkylations in the gas phase at the HF/6-31G\*\*//HF/3-21G level of theory.<sup>[6]</sup> According to these calculations, the INC involved in these reactions correspond to energy minima with a loose  $\pi$ -structure, where the alkyl cation and the aromatic ring lie in quasi-parallel planes and the formally charged carbon is centered above the ring centroid (the “ $\alpha$ -complex” in Figure 1). The stabilization energies of these  $\alpha$ -complexes relative to the separated components never exceed 13–15 kcal mol<sup>-1</sup>. The relative rotation of the two components of the complex is partially hindered by activation barriers from about 3 (*sec*-alkyl cation flipping over the arene ring) to about 10 kcal mol<sup>-1</sup> (the arene ring flipping over the *sec*-alkyl cation). Instead, the INC involved in the fragmentation of the  $\sigma$ -bonded alkylarenium intermediates (e.g. **I**) to the relevant arenium ion/alkene pair corresponds to an energy minimum with an even looser  $\pi$ -structure held together by a C<sup>+</sup>-H... $\pi$  interaction between the arenium ion and the double bond of the alkene moiety (the “ $\beta$ -complex” in Figure 1). No precise information about the relative stability of the  $\alpha$ - and  $\beta$ -complexes conceivably involved in the **I** fragmentation was provided. Nevertheless, following Audier’s indications,<sup>[6]</sup> the two complexes can be considered as almost equally stable.

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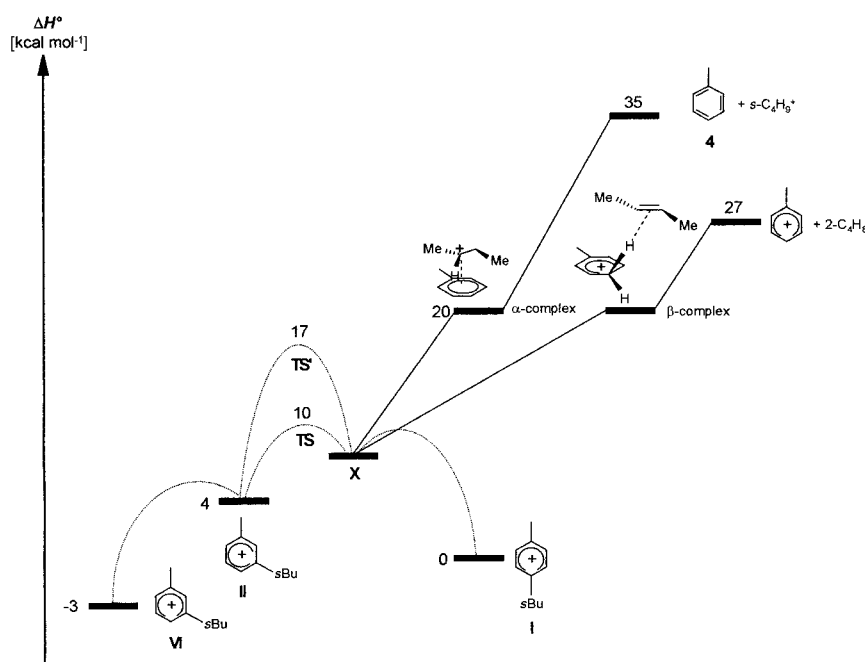


Figure 1. Schematic potential energy-reaction coordinate diagram for the gas-phase *sec*-butylation of toluene.

According to the model PES of Figure 1, the positional selectivity of gas-phase arene alkylations can be simply related to the different activation free energies for the conversion of the loosely-bound INC, either the  $\alpha$ - and  $\beta$ -complexes, to the isomeric  $\sigma$ -bonded alkylarenium intermediates. This view is severely questioned in the present kinetic investigation, based on a specifically designed experimental approach, which provides an alternative mechanistic model for this important class of reactions. The investigation required the synthesis of a tailor-made chiral arylalkane, that is (*S*)-(+)-1-*D*<sub>1</sub>-3-(*p*-tolyl)butane (**1<sup>S</sup>**), and the measure of its protonation-induced isomerization and dealkylation kinetics as a function of temperature ( $T = 100$ – $160$  °C). The reactions

**Abstract in Italian:** *La cinetica e la stereochimica di isomerizzazione unimolecolare di (S)-(+)-1-D<sub>1</sub>-3-(p-tolil)butano indotta da protonazione sono state studiate in fase gassosa nell'intervallo di temperatura da 100 a 160 °C. Il processo porta alla formazione quasi esclusiva del corrispondente isomero meta mediante migrazione del gruppo sec-butilico accompagnata dalla completa racemizzazione del centro chirale e parziale riarrangiamento dei suoi atomi di idrogeno. Questi risultati, insieme con i relativi parametri di attivazione, suggeriscono che l'isomerizzazione di (S)-(+)-1-D<sub>1</sub>-3-(p-tolil)butano indotta da protonazione avviene attraverso complessi alchil catione/toluene isomerici a bassa energia con strutture e stabilità definite (complessi tipo  $\eta^1$ ). L'esistenza e la struttura di tali complessi a bassa energia sono state confermate dai risultati di calcoli quantomeccanici di tipo ab initio su sistemi analoghi a livello MP2(full)/6-311++G\*\*//HF/6-31+G\*\*. Il ruolo chiave di questi intermedi finora trascurati emerge chiaramente dal confronto dei risultati presentati con quelli riguardanti la sec-butilazione diretta del toluene nelle stesse condizioni sperimentali.*

were carried out in CH<sub>4</sub> at 60 Torr in the presence of trace amounts of a radical scavenger (O<sub>2</sub>) and of a powerful base (B = (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>N). Protonation of **1<sup>S</sup>** was obtained by using the strong Brønsted acids C<sub>n</sub>H<sub>5</sub><sup>+</sup> ( $n = 1, 2$ ), which can be conveniently generated in the gas phase by  $\gamma$ -radiolysis of CH<sub>4</sub>.

## Experimental Section

**Materials:** Methane, [D<sub>4</sub>]methane, and oxygen were high-purity gases from UCAR Specialty Gases N.V., used without further purification. Triethylamine was purchased from ICON Services.

**(S)-(+)-1-D<sub>1</sub>-3-(p-Tolyl)butane (1<sup>S</sup>):** A solution of (*S*)-(+)-3-(*p*-tolyl)butan-1-ol (0.2 g) (gift by C. Fuganti and S. Serra of Politecnico di Milano)<sup>[9]</sup> in anhydrous diethyl ether (3 mL) was treated with sodium hydride (0.3 g).

The mixture was stirred and heated under reflux for 6 h. The suspension of the sodium alkoxide was cooled to  $-20$  °C with a dry ice bath and a solution of *p*-toluenesulphonyl chloride (1.5 g) in anhydrous diethyl ether (4 mL) was then added dropwise to the suspension. The reaction mixture was allowed to stand in the cold for 10 min, subsequently at room temperature for 45 min, and finally was heated under reflux for 2 h. The mixture was washed with diluted HCl, subsequently with water and dried over Na<sub>2</sub>SO<sub>4</sub>. The dried solution was added slowly to a suspension of LiAlD<sub>4</sub> (0.2 g) in anhydrous diethyl ether (4 mL). The mixture was heated under reflux for 8 h and then cooled and treated with ice-water to decompose excess of LiAlD<sub>4</sub>. After acidification with diluted H<sub>2</sub>SO<sub>4</sub> and extraction with diethyl ether (20 mL  $\times$  2), the organic extracts were washed with water, then dried and evaporated to give (*S*)-(+)-1-*D*<sub>1</sub>-3-(*p*-tolyl)butane (**1<sup>S</sup>**; 25 mg, *ee* 99%).

**(±)-2-(p-[D<sub>7</sub>]Tolyl)butane (1<sup>P</sup>):** This product was obtained by conventional Friedel–Crafts *sec*-butylation of [D<sub>7</sub>]toluene (Aldrich; D content: 97.6%) with 2-chlorobutane in the presence of aluminium chloride.<sup>[10]</sup>

**Purification of the starting substrates:** The synthetic products **1<sup>S</sup>** and **1<sup>P</sup>** were purified by preparative gas liquid chromatography (GLC) on: i) a 5 m  $\times$  4 mm (i.d.) stainless steel column packed with 10% Carbowax 20M on 80–100 mesh Chromosorb WAW at 90 °C; ii) a 5 m  $\times$  4 mm (i.d.) stainless steel column packed with 10% SP-1000 on 100–120 mesh Supelcoport at 90 °C. The chemical and optical purity of **1<sup>S</sup>** was verified by analytical GLC on the same chiral columns used for the analysis of its gas-phase protonation products (MEGADEX DACTBS- $\beta$  (30% 2,3-di-*O*-acetyl-6-*O*-*tert*-butyldimethylsilyl- $\beta$ -cyclodextrin in OV 1701, 25 m long, 0.25 i.d.,  $d_f = 0.25$   $\mu$ m),  $40 < T < 130$  °C, 2 °C min<sup>-1</sup>; CP-Chirasil-DEX CB, 25 m long, 0.25 mm i.d.,  $d_f = 0.25$   $\mu$ m),  $40 < T < 170$  °C, 5 °C min<sup>-1</sup>).

**Procedure:** The gaseous mixtures were prepared by conventional procedures with the use of a greaseless vacuum line. The starting chiral arene **1<sup>S</sup>** (or **1<sup>P</sup>**), the thermal radical scavenger O<sub>2</sub>, and the base (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>N (proton affinity (PA) = 234.7 kcal mol<sup>-1</sup>)<sup>[11]</sup> were introduced into carefully outgassed 130 mL Pyrex bulbs, each equipped with a break-seal tip. The bulbs were filled with CH<sub>4</sub> (or CD<sub>4</sub>) (60 Torr), cooled to liquid-nitrogen temperature, and sealed off. The gaseous mixtures were submitted to irradiation at a constant temperature (100–160 °C) in a <sup>60</sup>Co  $\gamma$ -source (dose:  $3.4 \times 10^4$  Gy; dose rate:  $2 \times 10^3$  Gy h<sup>-1</sup>, determined with a neopentane dosimeter). Control experiments, carried out at doses ranging from  $1 \times 10^4$  to  $1 \times 10^5$  Gy, showed that the relative yields of products are largely independent of the dose. The radiolytic products were analysed by GLC, with a Perkin-Elmer 8700 gas chromatograph equipped with a flame ionisation detector, on the same columns used to check the purity of the starting arene. The products were identified by comparison of their

retention volumes with those of authentic standard compounds and their identity confirmed by GLC-MS, using a Hewlett–Packard 5890A gas chromatograph in line with a HP 5970B mass spectrometer. Their yields were determined from the areas of the corresponding eluted peaks, using an internal standard (acetophenone) and individual calibration factors to correct for the detector response. Control experiments were carried out to rule out the occurrence of thermal fragmentation, isomerization, and racemization of the starting arene as well as of their isomeric products within the temperature range investigated.

The D-content and location in the radiolytic products were determined by GLC-MS, setting the mass analyser in the selected ion mode (SIM). The ion fragments at  $m/z$  119 [ $M - C_2H_4D$ ]<sup>+</sup>, 120 [ $M - C_2H_3$ ]<sup>+</sup>, and 149 [ $M$ ]<sup>+</sup> were monitored to analyse all the GLC-separated isomers of **1<sup>S</sup>** ( $\cong M$ ). The isomers of **1<sup>D</sup>** ( $\cong M^D$ ) were examined by using the fragments at  $m/z$  125 [ $M^D - C_2H_4D$ ]<sup>+</sup>, 126 [ $M^D - C_2H_3$ ]<sup>+</sup>, and 155 [ $M^D$ ]<sup>+</sup>. Toluenes **4**, obtained from **1<sup>S</sup>** and **1<sup>D</sup>**, were analysed by monitoring the ions at  $m/z$  91–93 and  $m/z$  96–100, respectively.

**Computational details:** Quantum-chemical ab initio calculations were performed using the Unix version of the Gaussian 98 set of programs<sup>[12]</sup> installed on a Alphaserver Compaq DS20E machine. The geometries of the investigated species have been optimised, by analytical-gradient techniques, at the HF/6-31+G\*\* level of theory, and the located critical points have been unambiguously characterized as true minima on the potential energy surface by computing, at the same computational level, the corresponding analytical vibrational frequencies. The latter values were used to calculate the zero-point vibrational energies (ZPE). The total energies of the HF/6-31+G\*\* optimised structures were finally refined by performing single-point calculations at the MP2/6-311++G\*\* level of theory using the “full” option so to include all the inner electrons in the calculation of the correlation energy.

## Results

**Radiolytic experiments:** Table 1 reports the composition of the irradiated systems as well as the identity and the yields of the major products, that is ( $\pm$ )-1-D<sub>1</sub>-3-(*m*-tolyl)butane (**2**), ( $\pm$ )-1-D<sub>1</sub>-2-(*m*-tolyl)butane (**3**), and toluene (**4**), obtained from gas-phase C<sub>n</sub>H<sub>5</sub><sup>+</sup> ( $n=1,2$ ) protonation of **1<sup>S</sup>** in the presence of trace amounts of (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>N (0.1 Torr). The table does not include other very minor products, that is deuterated ( $\pm$ )-2-(*o*-tolyl)butane and (*R*)-(-)-2-(*p*-tolyl)butane, whose overall yield never exceeds 3% of the reported products under all conditions. The numbers in Table 1 represent average values obtained from several separate irradiations carried out under the same experimental conditions; its reproducibility is expressed by the uncertainty level quoted. The ionic origin of the radiolytic products is demonstrated by the sharp decrease (over 80%) of their abundance as the (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>N concentration is raised from about 0.1 to about 0.5 mol %.

Products **2** and **3** arise from the isomerization of the *ipso*-protonated intermediate **I** of Scheme 1, while toluene **4**

derives from its de-*sec*-butylation. The nature itself of the products listed in Table 1, in particular their complete racemization and the extensive side-chain H-shift, excludes any significant methyl-group shift in **I** (path i in Scheme 1).

According to Scheme 1 and with the reasonable assumption that deprotonation of the relevant arenium ions by (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>N is fast, the rate constants for dealkylation ( $k_1$ ) and isomerization ( $k_2$  and  $k_3$ ) of **I** can be expressed as follows:

$$k_1 = \frac{Y_4 \ln [100/(100 - \Sigma)]}{\tau \Sigma} \quad (1)$$

$$k_2 = \frac{Y_2 \ln [100/(100 - \Sigma)]}{\tau \Sigma} \quad (2)$$

$$k_3 = \frac{Y_3 \ln [100/(100 - \Sigma)]}{\tau \Sigma} \quad (3)$$

where  $Y_i$  ( $= 100 \times [G_i/G(C_nH_5^+)]$ )<sup>[13]</sup> is the absolute percent yield of *i*-nth product relative to the starting **I**,  $\Sigma = Y_2 + Y_3 + Y_4$ , and  $\tau$  is the collision time between the arenium ions and B = (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>N ( $\tau = (k_{\text{coll}}[B])^{-1}$ ) at the given temperature.<sup>[14]</sup>

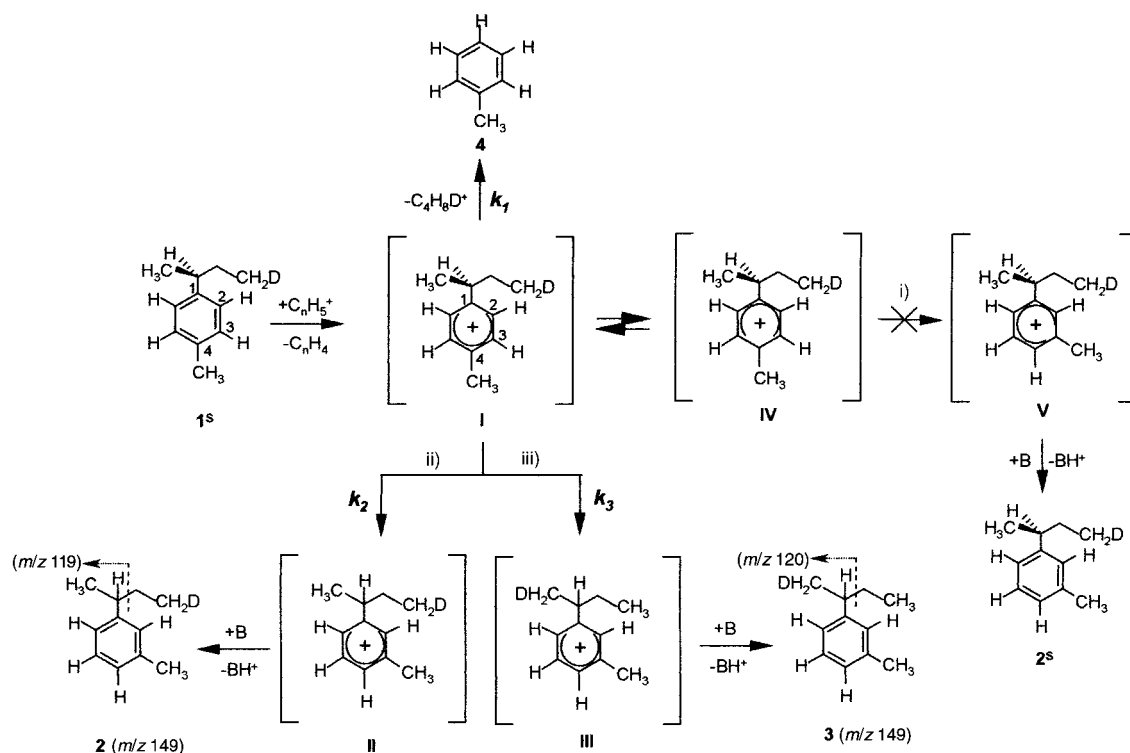
The Arrhenius plots of  $k_1$ ,  $k_2$ , and  $k_3$  over the 100–160 °C temperature range are reported in Figure 2. The linear curves obey the following equations:  $\log k_1 = (11.4 \pm 0.5) - [(10.6 \pm 0.9) \times 10^3]/2.303 RT$  ( $r^2 = 0.993$ );  $\log k_2 = (12.1 \pm 0.8) - [(11.1 \pm 1.5) \times 10^3]/2.303 RT$  ( $r^2 = 0.983$ ); and  $\log k_3 = (15.4 \pm 1.5) - [(17.7 \pm 2.8) \times 10^3]/2.303 RT$  ( $r^2 = 0.975$ ). The relevant activation parameters are calculated from the transition-state theory equation as:  $\Delta H^\ddagger_1 = 9.8 \pm 0.9$  kcal mol<sup>-1</sup> and  $\Delta S^\ddagger_1 = -8.7 \pm 2.7$  cal mol<sup>-1</sup> K<sup>-1</sup>;  $\Delta H^\ddagger_2 = 10.3 \pm 1.2$  kcal mol<sup>-1</sup> and  $\Delta S^\ddagger_2 = -5.3 \pm 3.6$  cal mol<sup>-1</sup> K<sup>-1</sup>; and  $\Delta H^\ddagger_3 = 16.9 \pm 3.1$  kcal mol<sup>-1</sup> and  $\Delta S^\ddagger_3 = +9.9 \pm 7.0$  cal mol<sup>-1</sup> K<sup>-1</sup>.

To shed some light upon the specific mechanism of isomerization of **I**, ancillary experiments were carried out under the same experimental conditions using C<sub>n</sub>D<sub>5</sub><sup>+</sup> ( $n=1,2$ ), as a Brønsted acid, and ( $\pm$ )-2-(*p*-[D<sub>7</sub>]tolyl)butane (**1<sup>D</sup>**), as the substrate. Indeed, as pointed out by Audier and co-workers,<sup>[15]</sup> occurrence of the  $\beta$ -complexes (Figure 1) in the fragmentation of deuterated **1<sup>D</sup>** would lead to appreciable D/H scrambling between the arene and the *sec*-butyl moieties. Gas-phase deuteration of **1<sup>D</sup>** with radiolytic C<sub>n</sub>D<sub>5</sub><sup>+</sup> yields the same product pattern of Table 1, with the obvious difference that 2-(*m*-[D<sub>7</sub>]tolyl)butane and 2-(*m*-[D<sub>6</sub>]tolyl)butane<sup>[16, 17]</sup> are formed instead of **2** and **3**, and [D<sub>8</sub>]toluene and [D<sub>7</sub>]toluene<sup>[16, 18]</sup> are formed instead of **4**. Careful mass spectrometric analysis of these products reveals that  $[2-(m-[D_7]\text{tolyl})\text{butane}]/[2-(m-[D_6]\text{tolyl})\text{butane}] = [[D_8]\text{toluene}]/[[D_7]\text{toluene}]$ . Besides, the 2-(*m*-[D<sub>7</sub>]tolyl)butane and 2-(*m*-[D<sub>6</sub>]tolyl)butane products exhibit just the same deuterium content in both the

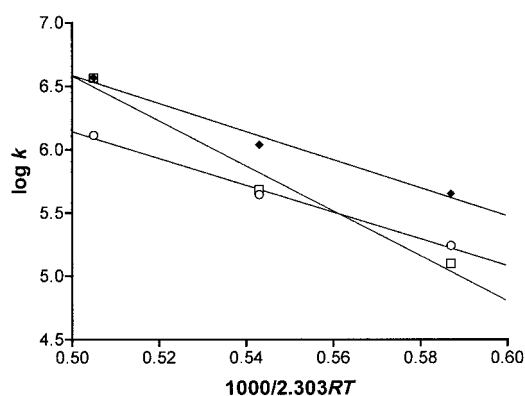
Table 1. Kinetics of gas-phase isomerization and dealkylation of protonated (*S*)-(+)-1-D<sub>1</sub>-3-(*p*-tolyl)butane **1<sup>S</sup>**.

System Comp. <sup>[a]</sup> <b>1<sup>S</sup></b> [Torr]	$T_{\text{reaction}}$ [°C]	$t_{\text{reaction}}$ ( $\tau \times 10^7$ s) <sup>[b]</sup>	$Y_2$ <sup>[c]</sup>	$Y_3$ <sup>[c]</sup>	$Y_4$ <sup>[c]</sup>	$\Sigma$ <sup>[d]</sup>	$k_1$ <sup>[e]</sup> ( $\times 10^{-5}$ s)	$k_2$ <sup>[e]</sup> ( $\times 10^{-5}$ s)	$k_3$ <sup>[e]</sup> ( $\times 10^{-5}$ s)
0.38	100	3.23	12.9	3.6	5.0	21.5	1.7 (5.24)	4.5 (5.65)	1.2 (5.10)
0.34	130	3.51	27.5	12.1	11.1	50.7	4.4 (5.64)	10.9 (6.04)	4.8 (5.68)
0.43	160	3.78	41.1	40.7	14.4	96.2	12.9 (6.1)	36.9 (6.57)	36.6 (6.56)

[a] CH<sub>4</sub>: 60 Torr, O<sub>2</sub>: 10 Torr; (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>N: 0.1 Torr. Radiation dose:  $3.4 \times 10^4$  Gy (dose rate:  $2 \times 10^3$  Gy h<sup>-1</sup>). [b] Reaction time,  $t$ , calculated from the reciprocal of the first-order collision constant between the relevant ionic adduct and (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>N (see text). [c]  $Y = 100 \times [G(\text{product})/G(C_nH_5^+)]$  ( $G$  values expressed as the number of molecule of the given species per 100 eV of energy absorbed by the gaseous mixture). [d]  $\Sigma = Y_2 + Y_3 + Y_4$ ; each value is the average of several determinations, with an uncertainty level of ca. 5%. [e]  $\log k$  in parentheses.



Scheme 1.

Figure 2. Temperature dependence of the  $k_1$  ( $\circ$ ),  $k_2$  ( $\blacklozenge$ ), and  $k_3$  ( $\square$ ) rate constants concerning the  $\text{I} \rightarrow \text{4}$ ,  $\text{I} \rightarrow \text{II}$ , and  $\text{I} \rightarrow \text{III}$  reactions, respectively.

corresponding parent  $[M^D]^+$  and  $[M^D - \text{ethyl}]^+$  fragment ions. These observations speak in favor of the same ionic precursor (i.e., the deuterated analogue of **I**) of both ring-deuterated 2-(*m*-tolyl)butanes and toluenes. The same results rule out any appreciable D/H scrambling between the aromatic ring and the side chain of deuterated **1<sup>D</sup>** during its isomerization and dealkylation and, therefore, the intermediacy of the noncovalent  $\beta$ -complex.

The conceivable occurrence of the noncovalent  $\alpha$ -complex of Figure 1 during **I** isomerization was ruled out by a second set of ancillary experiments. Thus, ionic *sec*-butylation of toluene was carried out at 70 Torr and in the 100–160 °C range using free *sec*-butyl cation as the electrophile. The relevant product distribution has been compared with that obtained from **I** isomerization carried out under identical

conditions. *sec*-Butyl ion attack on toluene leads to the formation of appreciable proportions of ( $\pm$ )-2-(*o*-tolyl)butane and ( $\pm$ )-2-(*p*-tolyl)butane (43–46% overall relative yield) besides ( $\pm$ )-2-(*m*-tolyl)butane (54–57%).<sup>[19]</sup> The almost complete absence of ( $\pm$ )-2-(*o*-tolyl)butane and (*R*)-(*S*)-2-(*p*-tolyl)butane from **I** isomerization ( $\geq 3\%$ ) excludes that both processes involve the intermediacy of the same noncovalent  $\alpha$ -complexes.

**Theoretical calculations:** The structure and the energetics of the stable intermediates involved in **I** isomerization were investigated by quantum-chemical ab initio calculations at the post-SCF level of theory. In order to reduce the calculation size, protonated *sec*-butyl benzene, instead of **I**, was considered. Exploration of the HF/6-31+G\*\* potential energy surface (PES) of protonated *sec*-butyl benzene around conceivable regions led to the location of only two distinct critical points, unambiguously characterized as true minima by analytical computation of the corresponding vibrational frequencies. The connectivity and the main geometrical parameters of these structures are shown in Figure 3 and their absolute and relative energies at the MP2(full)/6-311++G\*\*//HF/6-31+G\*\*+ZPE(HF/6-31+G\*\*) collected in Table 2.

## Discussion

**Energetics:** Gas-phase protonation of **1<sup>S</sup>** by the strong Brønsted acids  $\text{C}_n\text{H}_5^+$  ( $n=1,2$ ) is an exothermic process yielding the corresponding arenium ion protomers.<sup>[16]</sup> Forma-

Table 2. Computed MP2(full) absolute and relative energies (including ZPEs) and zero-point energies (ZPE) of intermediates involved in isomerization and fragmentation of protonated *sec*-butylbenzene.

Structure	$E$ [au]	ZPE [kcal mol <sup>-1</sup> ]	$\Delta E$ [kcal mol <sup>-1</sup> ]
benzene	-231.696585	67.27	
<i>sec</i> -butyl ion	-157.107375	77.93	28.74
benzenium ion	-231.982775	74.04	
<i>trans</i> -2-butene	-156.820785	72.00	29.84
$\sigma$ -complex	-388.856944	149.71	0.00
$\eta^1$ -complex	-388.833906	146.67	11.41

tion of the *ipso*-protonated intermediate **I** is estimated to be exothermic by 59 ( $n=1$ ) and 26 kcal mol<sup>-1</sup> ( $n=2$ ).<sup>[11]</sup> The excess energy imparted to the ion **I** and the C<sub>n</sub>H<sub>4</sub> fragments by the exothermicity of their formation process is efficiently dissipated by multiple unreactive collisions with the bulk CH<sub>4</sub> gas. As illustrated in Scheme 1, the *ipso*-intermediate **I** may isomerize to ions **II** and **III**, with complete racemization of the *sec*-butyl group, or undergo de-*sec*-butylation to give eventually the products of Table 1.

With the reasonable assumption that the proton affinity (PA) of **1<sup>s</sup>** at C(1) is comparable with that of *p*-xylene (PA = 190 kcal mol<sup>-1</sup>),<sup>[11]</sup> the heat of formation of **I** can be estimated as 161 kcal mol<sup>-1</sup>. In the same way, the heat of formation of **II** (and **III**) can be estimated as 165 kcal mol<sup>-1</sup>, whereas that of **VI** (Figure 2) is about 158 kcal mol<sup>-1</sup>.<sup>[11, 16]</sup> Unimolecular dissociation of **I** to give the separated toluene/*sec*-butyl cation and the *p*-toluenium ion/2-butene pairs can be calculated to be about 35 and 27 kcal mol<sup>-1</sup> endothermic, respectively (Figure 1).<sup>[11]</sup>

Despite the obvious structural, electronic, and temperature differences, these values well compare with the relevant  $\Delta E$  values of Table 2. Both sets of dissociation energies are consistent with the experimentally observed predominant release of the C<sub>7</sub>H<sub>9</sub><sup>+</sup>/C<sub>4</sub>H<sub>8</sub> pair from dissociation of **I** and of the C<sub>4</sub>H<sub>9</sub><sup>+</sup>/C<sub>6</sub>H<sub>6</sub> one from protonated *sec*-butyl benzene.<sup>[5, 15]</sup>

**The isomerization mechanism:** Having excluded any significant occurrence of path i of Scheme 1, the formation of ( $\pm$ )-1-D<sub>1</sub>-3-(*m*-tolyl)butane (**2**) from **1<sup>s</sup>** must necessarily arise from the **I** → **II** isomerization involving the complete racemization of the chiral *sec*-butyl moiety (path ii of Scheme 1). *sec*-Butyl group racemization is accompanied by partial 1,2-H shift, as demonstrated by the concomitant formation of ( $\pm$ )-1-D<sub>1</sub>-2-(*m*-tolyl)butane (**3**) (path iii of Scheme 1).<sup>[5, 15]</sup> These findings point to intermediate structures along the **I** → **II/III** reaction coordinate characterized by extensive C<sub>ring</sub>-C<sub>alkyl</sub> bond cleavage.<sup>[5, 6, 17]</sup> However, as pointed out in the Results Section,

these loosely bound structures do not correspond to the noncovalent  $\alpha$ - and  $\beta$ -complexes of Figure 1.

This conclusion is corroborated by the evident gap between the measured activation enthalpies of the **I** → **II** ( $\Delta H^\ddagger_2 = 10.3 \pm 1.2$  kcal mol<sup>-1</sup>) and **I** → **III** isomerizations ( $\Delta H^\ddagger_3 = 16.9 \pm 3.1$  kcal mol<sup>-1</sup>) and the HF/6-31G\*\*//HF/3-21G-computed enthalpy difference between **I** and the noncovalent  $\alpha$ - and  $\beta$ -complexes of Figure 1 (ca. 20 kcal mol<sup>-1</sup>). This discrepancy clearly indicates that the **I** → **II** and **I** → **III** isomerization reactions proceed through transition structures placed well below the noncovalent  $\alpha$ - and  $\beta$ -complexes on the relevant PES (i.e., **TS** and **TS'** in Figure 1, respectively). The complete racemization and the temperature-dependent 1,2-H shift accompanying the *sec*-butyl group C(1) → C(2) motion in **I** provide mutually reinforcing pieces of evidence for the presence of long-lived intermediates around the **TS** and **TS'** transition structures which allow for several rotations and bond vibrations in the *sec*-butyl moiety before  $\sigma$ -bonding to **II** or **III** (i.e., the **X** complex of Figure 1).

The activation parameters of the **I** → **II** isomerization ( $\Delta H^\ddagger_2 = 10.3 \pm 1.2$  kcal mol<sup>-1</sup> and  $\Delta S^\ddagger_2 = -5.3 \pm 3.6$  cal mol<sup>-1</sup> K<sup>-1</sup>) assign to this **X** complex a low-energy, tight structure, where free mutual motions of the *sec*-butyl group and the toluene components is severely hampered by intense interactions. This species is identified as the methylated analogue of the  $\eta^1$ -type complex of Figure 3.<sup>[20]</sup> Neighboring-

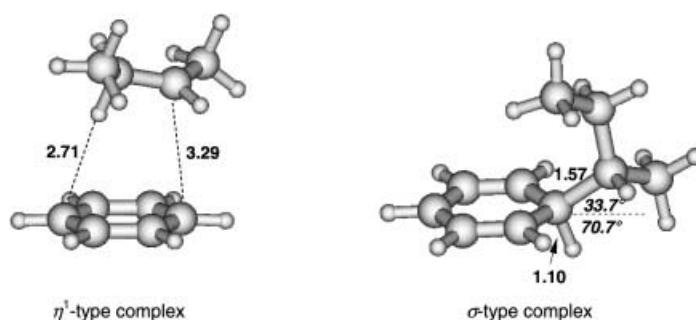
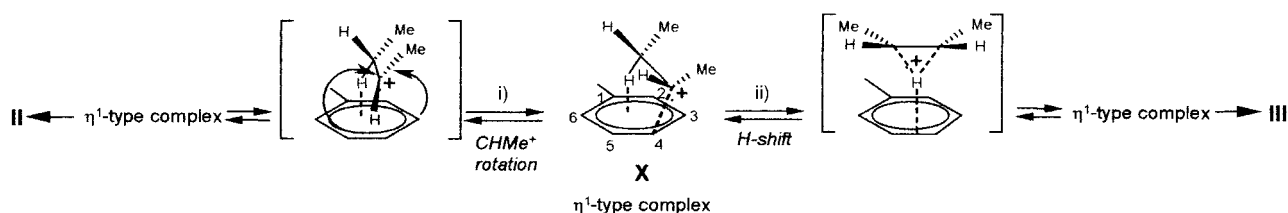


Figure 3. HF/6-31+G\*\*-optimized structures and main geometrical parameters of the stable  $\sigma$ - and  $\eta^1$ -type complexes located on the potential energy surface (PES) of protonated *sec*-butyl benzene (bond lengths in Å; angles in ° (in italic)).

group effects in the *sec*-butyl moiety of the  $\eta^1$ -complex may induce CHMe<sup>+</sup>-group flipping so that the formally vacant p-orbital can undergo attack on both its sides from the adjacent ring-C(3) and -C(5) centers (path i of Scheme 2).

The activation parameters of the **I** → **III** isomerization ( $\Delta H^\ddagger_3 = 16.9 \pm 3.1$  kcal mol<sup>-1</sup> and  $\Delta S^\ddagger_3 = +9.9 \pm 7.0$  cal mol<sup>-1</sup> K<sup>-1</sup>) point to an additional higher-energy route



Scheme 2.

to the **X** complex, involving a comparatively looser transition structure **TS'** where the interaction between the *sec*-butyl group and the toluene  $\pi$ -system is enough weakened to allow 1,2-H shift in the *sec*-butyl moiety (path ii of Scheme 2). The 1,2-H shift in the *sec*-butyl moiety may allow attack from the adjacent ring-C(3) centers with formation of **III**. The isomerization sequences, proposed in Scheme 2, account for all the experimental findings, including the lack of any significant formation of both ( $\pm$ )-2-(*o*-tolyl)butane and (*R*)-(-)-2-(*p*-tolyl)butane from protonation of **1**<sup>5</sup>. The  $\eta^1$ -type **X** complexes involved in the isomerization pathways are characterized by defined structure and stability arising from the spatial relationship between the specific  $C_{\text{arom}} \cdots C^+$  interaction and the ring substituent group. In this view, the *sec*-butyl ion/toluene potential energy surface can be characterized by the intermediacy of isomeric *para*, *meta*, and *ortho*  $\eta^1$ -type complexes, which may control the subsequent formation of the corresponding  $\sigma$ -intermediates and, hence, determine the positional selectivity of the process (see below).<sup>[21]</sup>

**The dealkylation mechanism:** According to Figure 1, the energy required for the unimolecular de-*sec*-butylation of **I** (27 kcal mol<sup>-1</sup>) largely exceeds the activation enthalpy measured for the formation of toluene **4** from **I** ( $\Delta H^\ddagger_1 = 9.8 \pm 0.9$  kcal mol<sup>-1</sup>). This discrepancy, coupled with the negative activation entropy value ( $\Delta S^\ddagger_1 = -8.7 \pm 2.7$  cal mol<sup>-1</sup> K<sup>-1</sup>), excludes any conceivable unimolecular **I** fragmentation to **4**, while supporting the direct formation of toluene by the exothermic bimolecular  $\beta$ -elimination process induced by (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>N attack at the side chain of **I** ( $\Delta H_{\text{elim}} = -20.6$  kcal mol<sup>-1</sup>).<sup>[11]</sup>

**Comparison with the gas-phase *sec*-butyl cation attack on toluene:** Formation of the tightly-bound  $\eta^1$ -type complexes in the isomerization of **I** (Scheme 2) rises some questions about the role of these intermediates in determining the substrate and positional selectivity of the gas-phase ionic alkylation of arenes. Whichever alkylation route is considered, either by attack of the alkyl cation on the arene or by addition of the arenium ion on the alkene, the classical mechanistic model involves the preliminary formation of a loosely-bound INC, either the  $\alpha$ - and  $\beta$ -complex (Figure 1), acting as a microscopic reaction “vessel” wherein the reactants are confined by electrostatic forces. According to this model, the  $\alpha$ - and  $\beta$ -complexes may easily equilibrate if separated by a low activation barrier. The substrate selectivity of the alkylation reaction essentially reflects the competition between the collisional stabilization of the loosely-bound INC and their fragmentation. The positional selectivity reflects instead the different activation free energies for the conversion of the loosely-bound INC to the isomeric  $\sigma$ -bonded arenium structures.

A careful comparison of the present experimental results with those from the direct *sec*-butylation of toluene seems to put into question this widely accepted model. Indeed, at 24 °C, the positional selectivity of the *sec*-butyl cation toward toluene is thought to be represented most faithfully by the relative population of the isomeric  $\sigma$ -bonded arenium ions, measured at the highest pressures (710 Torr; *ortho*: 42 %;

*meta*: 30 %; *para*: 28 %).<sup>[19]</sup> When the pressure is lowered to 70 Torr at the same temperature, a considerable change in the isomeric distribution of the alkylated products (*ortho*: 35 %; *meta*: 47 %; *para*: 18 %) is observed, which is attributed to a facile interconversion among the isomeric  $\sigma$ -bonded arenium ions.

The present study on the gas-phase isomerization of **I** indicates that these arenium ions are long lived at 70 Torr and within the 100–160 °C range. Indeed, the **I**  $\rightarrow$  **II** isomerization rate constants measured within this temperature range ( $k_2 = 4.5 \times 10^5$  s<sup>-1</sup> (at 100 °C);  $1.1 \times 10^6$  s<sup>-1</sup> (at 160 °C); Table 1) indicate that **I** undergoes from about 1600 (160 °C) to about 4000 (100 °C) collisions with CH<sub>4</sub> before isomerizing to **II**.<sup>[22]</sup> Thus, at 70 Torr and  $T \geq 160$  °C, the **I** arenium ion lives long enough to be in thermal equilibrium with the bulk gas before reacting. The same conclusion is valid a fortiori when isomeric  $\sigma$ -bonded arenium ions are generated by *sec*-butylation of toluene at room temperature and in the 70–710 pressure range.<sup>[19]</sup> Accordingly, the relative population of these ions should depend only on the temperature and not on the bulk gas pressure.

The large pressure effect on the isomeric distribution of products from gas-phase *sec*-butylation of toluene ( $T = 24$  °C)<sup>[19]</sup> can find a rationale only by acknowledging the intermediacy of isomeric  $\eta^1$ -type complexes with lifetimes comparable with their collision time with the bulk gas at 70–710 Torr ( $5 \times 10^{-10}$ – $5 \times 10^{-11}$  s).<sup>[14, 23]</sup>

In this frame, the positional selectivity of the gas-phase *sec*-butylation of toluene, a model reaction for electrophilic aromatic substitutions, is determined by the relative population of isomeric  $\eta^1$ -type complexes and the activation free energies for their conversion to the relevant  $\sigma$ -bonded arenium ions. When collisional cooling of the  $\eta^1$ -type complexes is efficient (high pressure), the reaction is essentially controlled by enthalpy factors favoring the formation of their *ortho* and *para* isomers and their conversion to the corresponding  $\sigma$ -arenium intermediates. When instead collisional cooling of the  $\eta^1$ -type complexes is not so efficient (low pressure), their relative population and conversion to the corresponding  $\sigma$ -arenium ion can be significantly altered by the contribution of the entropic factors.

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