Gas-Phase Methylenation of Benzene and Substituted Benzenes by $C_2H_5O^+$ Ion. A Novel Electrophilic Aromatic Substitution

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Abstract: Ion cyclotron resonance spectrometric investigation of the ion–molecule reactions of the $CH_2O^+CH_3$ ion, formed from fragmentation of dimethyl ether, with aromatic substrates led to the study of a novel electrophilic aromatic methylenation reaction: $ArH + CH_2OCH_3^+ \rightarrow ArCH_2^+ + CH_3OH$. Methylenation of toluene, as shown in competition experiments with benzene and using deuterated derivatives, proceeds with low, but significant substrate selectivity and statistical positional distribution. The results are compared with other electrophilic aromatic substitution reactions.

In previous studies using ion cyclotron resonance (icr) spectrometry, we have studied gas-phase aromatic nitration, acetylation, protonation, and alkylation (eq 1–4)[1] and found distinct, although generally low, substrate selectivity in the reactions.

$$CH_2ONO_2^+ + ArH \longrightarrow ArHONO^+ + CH_2O \qquad (1)$$

$$(CH_3CO)_2^+ + ArH \longrightarrow ArHCH_3CO^+ + CH_3CO \qquad (2)$$

$$C_3H_7^+ + ArH \longrightarrow ArH_2^- + C_3H_6 \qquad (3)$$

$$i\text{-}C_3H_7I^+ + Ar \longrightarrow i\text{-}C_3H_7Ar^+ + I\cdot \qquad (4)$$

The substituent rate effects in reactions 2–4 were typical of electrophilic attack on the aromatic substrate, but reaction 1 was found, quite unexpectedly, to show a pattern of substituent effects clearly suggesting the nucleophilic nature of the attack. In these studies the question of positional selectivity could not be elucidated, since the leaving group arises from the ionic reactants and not from the aromatic substrates.

It is, however, of considerable interest to study positional as well as substrate selectivity in gas-phase aromatic substitution reactions.

The gas-phase ion chemistry of isomeric $C_2H_5O^+$ ions (m/e 45) has been previously studied in great detail using various techniques.[2–7] It has been established that $CH_2O^+CH_3$ is the major isomeric ion arising from the fragmentation of methyl ether. This ion has been shown to undergo methyl transfer and hydride abstraction reactions with its parent neutrals. We wish to report now a novel gas-phase aromatic methylenation reaction using the $CH_2O^+CH_3$ ion in which positional as well as substrate selectivity can be studied.

Results and Discussion

In the icr spectrum of dimethyl ether at 12.8 eV and 5×10^{-6} Torr, we observed only three ions in significant abundance, m/e 45, 46, and 47. The secondary ion, m/e 47, arises from a proton-transfer reaction.

$$CH_3\overset{+}{O}CH_3 + CH_3OCH_3 \longrightarrow (CH_3)_2\overset{+}{O}H + C_2H_5O \qquad (5)$$

When benzene is introduced through a second sample inlet, increasing the total pressure to 8×10^{-6} Torr, an additional secondary ion is observed at m/e 91 (m/e 96 for benzene-d_6). Double resonance experiments confirm the occurrence of reactions 6 and 7.

$$CH_2\overset{+}{O}CH_3 + C_6H_6 \longrightarrow C_7H_7^+ + CH_3OH \qquad (6)$$

$$CH_2\overset{+}{O}CH_3 + C_6D_6 \longrightarrow C_7D_5H_2^+ + CH_3OD \qquad (7)$$

The net result is transfer of a methylene group from $CH_2O^+CH_3$ to benzene with replacement of a ring proton, *i.e.*, the methylenation of benzene. This is a new type of aromatic substitution reaction which has not previously been observed in the gas-phase chemistry of the $CH_2O^-CH_3$ ion and is without precedent in solution chemistry. Likewise, using toluene, toluene-α-d_3, and toluene-d_5, the following reactions were verified by double resonance experiments.

$$CH_2\overset{+}{O}CH_3 + C_6H_5CH_3 \longrightarrow C_8H_9^+ + CH_3OH \qquad (8)$$

$$CH_3\overset{+}{O}CH_2 + C_6H_5CD_3 \longrightarrow C_8H_6D_3^+ + CH_3OH \qquad (9)$$

$$CH_3\overset{+}{O}CH_2 + C_6D_5CH_3 \longrightarrow C_8H_5D_4^+ + CH_3OD \qquad (10)$$

Since a deuteron is replaced in $C_6D_5CH_3$ but not in $C_6H_5CD_3$, the substitution must be occurring at the ring positions of toluene. Our results also show that the leaving hydrogen atom does not come from the $CH_2O^+CH_3$ ion and that there is no hydrogen exchange between this ion and the aromatic neutral substrate.

In order to eliminate the possibility that the reaction is not proceeding *via* methylenation by the $CH_2O^+CH_3$ ion but by methylation (a reaction observed in solution chemistry of the stable methoxy carbonium ion[8]) with subsequent loss of molecular H_2, benzene and toluene were reacted with methyl ether-d_3. Double resonance results revealed only the following reactions.

$$CD_3\overset{+}{O}CH_2 + C_6H_6 \longrightarrow C_7H_7^- + CD_3OH \qquad (11)$$

$$CH_3\overset{+}{O}CD_2 + C_6H_6 \longrightarrow C_7H_5D_2^+ + CH_3OH \qquad (12)$$

$$CD_3\overset{+}{O}CH_2 + C_6H_5CH_3 \longrightarrow C_8H_9^+ + CD_3OH \qquad (13)$$

$$CH_3\overset{+}{O}CD_2 + C_6H_5CH_3 \longrightarrow C_8H_7D_2^+ + CH_3OH \qquad (14)$$

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(1) (a) R. C. Dunbar, J. Shen, and G. A. Olah, *J. Amer. Chem. Soc.*, **94**, 6862 (1972); (b) J. Shen, Ph.D. Thesis, Case Western Reserve University, Cleveland, Ohio, 1972.

(2) M. S. B. Munson and J. L. Franklin, *J. Phys. Chem.*, **68**, 3193 (1964).

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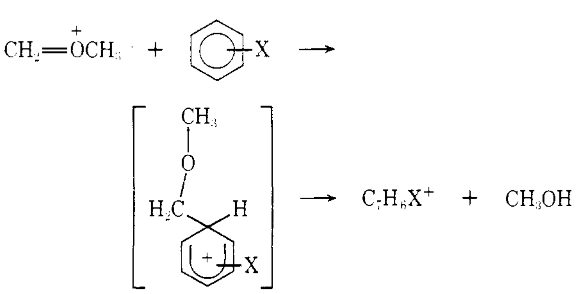
(6) F. W. McLafferty and H. D. R. Schuddemage, *ibid.*, **91**, 1866 (1969).

(7) (a) J. L. Beauchamp and R. C. Dunbar, *ibid.*, **92**, 1477 (1970); (b) J. L. Beauchamp, Ph.D. Thesis, Harvard University, Cambridge, Mass., 1968.

(8) G. A. Olah and J. J. Svoboda, *Synthesis*, 53 (1973).

Reactions 11–14 conclusively demonstrate that the reaction is proceeding by methylenation and not methylation.

As always in studies of this type, it should be emphasized that these results provide only indirect information about the details of the reaction, and drawing hypothetical transition states could be only speculation. Still it is attractive to postulate that at some point in these reactions the methylene carbon forms a σ bond with a ring carbon of arenium ion nature.



(15)

Such a transition state has precedent in analogous transition states which have been postulated in several previous deuterium-labeled ion–molecule reactions studies,[9] although the reaction reported here clearly must differ in important respects.

The methanol leaving group has a very low heat of formation, −50 kcal/mol. The heat of formation of $CH_2O^+CH_3$ is somewhat uncertain, recent estimates ranging around 155 kcal/mol.[10] Assuming the benzylic structures for the product ions, reaction 6 is exothermic by about 9 kcal/mol and reaction 8 is exothermic by about 18 kcal/mol. If the product ion in reaction 6 has the tropylium structure, the reaction will be exothermic by about 16 kcal/mol. Likewise, reaction 8 may be slightly more exothermic assuming that the product ion is the methyltropylium ion. In general, it seems clear that all of these methylenation reactions are substantially exothermic.

Competition experiments between different aromatic substrates were performed by admitting mixtures of the two aromatic compounds through a second sample inlet to the icr cell containing a constant pressure of dimethyl ether. In this way, relative reaction rates were determined competitively by comparing abundances of the two methylenated product ions. The usual mass corrections were made[11,12] and the relative partial pressures of the two aromatic compounds were determined from the single resonance peak intensities using relative impact cross sections at 70 eV obtained or calculated from the literature.[13] In each case in which methylenation was significant, it was verified by standard double resonance ejection techniques that $C_2H_5O^+$ was the only important precursor of the methylenation product.

Competition experiments using C_6H_6–C_6D_6 and $C_6H_5CH_3$–$C_6D_5CH_3$ show a kinetic hydrogen isotope effect of $k_H/k_D = 2.0$. However, when toluene and toluene-α-d_3 were compared, no kinetic hydrogen isotope effect was observed. This further supports our observation that the methylenation is not occurring at the side chain but at the aromatic ring.

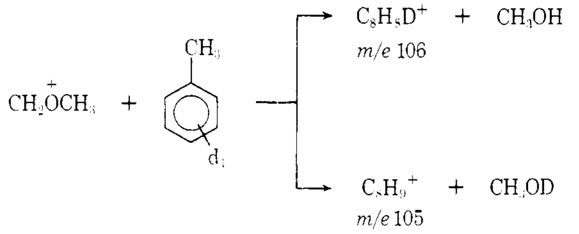
In a similar fashion, competition experiments were performed using other substituted benzene derivatives. C_6D_6 was used in place of benzene in competition with alkyl benzenes, since the methylenated benzene, $C_7H_7^+$, appears at the same *m/e* as the fragment ion of alkyl substituted benzenes. To increase the sensitivity of the experiments and to cross check results, toluene-α-d_3 and benzene-d_6 were both examined in competition with ethyl- and propylbenzene in separate experiments. The relative rates of methylenation of benzene derivatives are summarized in Table I.

Table I. Relative Rates of Methylenation of Benzene and Substituted Benzenes

ArH	K_{ArH}/k_B	ArH	K_{ArH}/k_B
C_6H_6	1.0	C_6H_5F	0.10 ± 0.05
C_6D_6	0.50 ± 0.05	$C_6H_5CF_3$	0.0 (<0.05)
$C_6H_5CH_3$	1.8 ± 0.1	$C_6H_5C_2H_5$	5 ± 1
$C_6H_5CD_3$	1.9 ± 0.1	$C_6H_5C_3H_7$	5 ± 1
$C_6D_5CH_3$	0.9 ± 0.1		

The relative reaction rates increase when the substituent is changed from methyl to ethyl or *n*-propyl. However, fluorine and particularly CF_3 substituents decrease the substitution rate substantially. These observations suggest that gas-phase aromatic methylenation is electrophilic in nature.

In order to determine if there is any positional selectivity in the methylenation of toluene, ortho, meta, and para deuteriotoluenes were methylenated with the $CH_2O^+CH_3$ ion (eq 16). If the substitution occurs at an unlabeled position, the product ion will occur at *m/e* 106, and if it occurs at a labeled position, the product ion is *m/e* 105. The results are summarized in Table II.



(16)

The results demonstrate that there is not experimentally significant positional selectivity in the methylenation of toluene. This lack of positional selectivity can be explained either by a lack of selectivity in the site of attack of the entering cation or by scrambling of the deuterium label around the ring prior to elimination. It is known that hydrogen scrambling in aromatic cations is rapid at low electron energies where ions of low internal energies and long lifetimes are present,[14] as is also the case under the mild conditions of icr. However, nothing is known in the gas phase about the possibility of proton scrambling in arenium-type cations of the type represented by the transition state in eq 15. (Such intramolecular

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(9) S. E. Buttrill, Jr., *J. Amer. Chem. Soc.*, **92**, 3560 (1970); J. L. Beauchamp, *ibid.*, **91**, 5925 (1969); M. C. Caserio and J. L. Beauchamp, *ibid.*, **94**, 2638 (1972).

(10) See C. D. Finney and A. G. Harrison, *Int. J. Mass Spectrom. Ion Phys.*, **9**, 221 (1972).

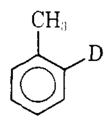
(11) (a) A. G. Marshall and S. E. Buttrill, Jr., *J. Chem. Phys.*, **52**, 2752 (1970); (b) S. E. Buttrill, Jr., *ibid.*, **50**, 4125 (1969); (c) M. B. Comisarow, *ibid.*, **55**, 205 (1971); (d) R. C. Dunbar, J. Shen, and G. A. Olah, *ibid.*, **56**, 3794 (1972).

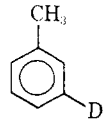
(12) D. Holtz, J. L. Beauchamp, and J. R. Eyler, *J. Amer. Chem. Soc.*, **92**, 7045 (1970).

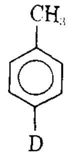
(13) (a) J. W. Otvos and D. P. Stevenson, *ibid.*, **78**, 546 (1956); (b) F. W. Lampe, J. L. Franklin, and F. H. Field, *ibid.*, **79**, 6129 (1957).

(14) A. N. H. Yeo and D. H. Williams, *ibid.*, **91**, 3582 (1969).

Table II. Relative Positional Reactivities in Toluene


A


B


C

Isomeric toluene	$I_{105}/(I_{105} + I_{106})^a$
A	0.16 ± 0.02
B	0.19 ± 0.02
C	0.18 ± 0.02

[a] The isotopic purity of the compounds was determined by nmr to be 92% ortho, 94% meta, and 92% para, and a correction was made to the m/e 105 peak height to allow for the contribution from undeuterated toluene.

isomerization in arenium ions, prior to deprotonation, has been suggested in solution chemistry.[15])

Conclusion

The observed aromatic methylenation reaction is characterized by low, but significant, substrate selectivity. At the same time no positional selectivity was found in the case of toluene.

Little work has been carried out in determining substrate and positional selectivities in gas-phase electrophilic substitution reactions. In the gas-phase radiation-induced isopropylation of benzene and toluene,[16] statistical substrate as well as positional reactivity was observed. It was suggested that the reactant $C_3H_7^+$ ion initially forms an energetically excited π complex which then transforms statistically into isomeric σ complexes. In the gas-phase tritiation of aromatics with the HeT^+ ion, Cacace, *et al.*,[17] have observed low but measurable substrate and positional selectivity. It was proposed that the low selectivities were caused by highly energetic HeT^+ ions. In electrophilic aromatic substitution in solution chemistry, low substrate selectivity with simultaneous high positional selectivity is observed for reactions involving electrophiles of high reactivity. It was proposed by Olah[18] that the mechanism of these electrophilic aromatic substitutions proceeds by initial π-complex-like aronium ion formation followed by conversion into the isomeric σ complexes (arenium ions). With high-reactivity electrophiles, such as the nitronium ion, fast π-complex formation gives the observed low substrate selectivities while the subsequent formation of σ complexes determines the positional selectivities. On the other hand, in selective reactions with weaker electrophiles, substrate selectivity is greater and the "late" transition states resemble the intermediates, resulting in a greater amount of para substitution.

The conditions under which ion–molecule reactions are carried out in the icr spectrometer are milder, in terms of internal and translational excitation of reactants, than those of gas-phase radiolysis or tritiation, so that of the techniques which have been applied to gas-phase study of aromatic substitution icr is probably most closely comparable to solution-phase studies. The observation of significant substrate selectivity indicates that under icr conditions the rate-determining step of the reaction is not fully encounter controlled. We believe that the present results are consistent with the solution-phase mechanistic concepts involving initial formation of π-complex-like aronium ions followed by conversion into σ complexes (arenium ions). Within this picture, the lack of positional selectivity can be understood as reflecting either statistical formation of σ complexes or hydrogen scrambling in the σ complex.

Experimental Section

Our studies were carried out with a Varian ICR-9 spectrometer equipped with the standard flat cell. Double resonance experiments were performed by irradiating in the analyzer region with a radiofrequency voltage of 0.032 V and directly monitoring the decrease in product ion signal. Pressures were measured from the VacIon pump current. A double inlet system was used to admit samples. Dimethyl ether was admitted through one inlet system, providing the reactant ions, while aromatic substrates were admitted through the second inlet. The competition reactions were carried out using the lowest possible pressures (8×10^{-6} Torr) and electron energy (12.8 eV). Other instrumental parameters were: trapping voltage, 0.15 V, and drift voltages, a few tenths of a volt or less. In most cases reagent grade chemicals were used without further purification and no extraneous peaks were observed. Toluene-α-d_3 was prepared according to the method of Renaud and Leitch.[19] Isotopic purity was high (95%) as analyzed by nmr and mass spectrometry (isotopic purities given as mole per cent of the compound labeled as indicated). Toluene-d_5 was prepared by first brominating C_6D_6 (yield 99.5%) and then methylating the bromobenzene-d_5. The isotopic purity obtained for toluene-d_5 was >99%. *o*, *m*, and *p*-toluene-d_1 were prepared according to the method of Best and Wilson.[20] The methyl ether-d_3 was prepared by placing methyl bromide-d_3 (2.5 g), sodium methoxide (1.38 g), and *p*-xylene (10 ml) in a bomb and heating at 100° for 18 hr. The isotopic purity of the methyl ether-d_3 was 98% as determined by low-pressure icr at 70 eV electron energy.

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, to the Research Corporation under a Frederick Gardner Cottrell grant, and to the National Science Foundation for partial support of this research.

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(18) For a review, see G. A. Olah, *Accounts Chem. Res.*, **4**, 240 (1971).

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