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Dear Sir,

## Chemical Ionization of *n*-Propyl Phenyl Ether with $D_2O$ Reagent Gas. A Test of Statistical Models

In a pioneering study two decades ago, Benoit and Harrison[1] reported the exchange of $D^+$, deposited on *n*-propyl phenyl ether (*n*PrOPh = M) by chemical ionization (CI), with the CH hydrogens of the side chain. The fragmentation pattern of $MD^+$ revealed not only this exchange, but also transposition of hydrogen within the propyl group, with no apparent participation of the ring hydrogens. A few years later, one of us suggested that the CI behavior of *n*PrOPh could be explained in terms of the intermediacy of [phenol isopropyl cation] ion–neutral complexes. Since that time, other examples of such exchange have been described, which have been explained in an analogous fashion.[3]

Previously, we examined metastable ion data for $CD_4$ CI on *n*PrOPh and its deuterated analogues in order to distinguish between alternative mechanistic hypotheses.[4] Protonated phenol is the only decomposition product seen in the mass-analyzed ion kinetic energy (MIKE) spectrum. In the preferred mechanism, exchange of the CI hydron with the chain and randomization within the chain compete with decomposition, and neither achieves complete equilibration. The distribution of deuterium in the fragment ions was analyzed using steady-state kinetics. Values of five branching ratios (including isotope effects) were extracted from the data. Subsequently, we used these values to make predictions regarding $CH_4$ CI of the same deuterated compounds and found only a qualitative agreement between predicted fragment ion ratios and our experimental data.[5] We attributed the quantitative differences to an insufficient level of detail in our mechanism, and also to possible shortcomings in applying steady-state kinetics to metastable ion decompositions.

Recently, Bogdanov *et al.*[6] (referred to below as BMIN) proposed a much simpler model, in which [cyclohexadienone isopropyl cation] complexes form in competition with [phenol isopropyl cation] complexes. In our own previous work we had assumed that CI on the benzene ring produces ions that did not contribute significantly to the metastable ion spectra.[4,5] In the BMIN model, by contrast, deposition of $D^+$ on the ring or on the oxygen are both presumed to lead to reactive ions. The BMIN model has several appealing features, one of which is that it has no adjustable parameters. Fragment ion ratios can be predicted by means of simple statistics, which give excellent fits for *m/z* 95:96:97 ratios in the $D_2O$ CI of unlabeled *n*PrOPh (**1**) and of $CH_3CD_2CH_2OPh$ (**2**). Here we compare the predictions of the BMIN model (and two related statistical models) with $D_2O$ CI data for seven other chain-deuterated analogues of *n*PrOPh. We regretfully conclude that none of the mechanistic schemes that have so far been advanced is adequate to predict the *m/z* 95:96:97 relative ion abundances with accuracy.

Mass-analyzed ion kinetic energy (MIKE) spectra and *B/E* scans were recorded on a VG ZAB reverse geometry (B–E) double-focusing mass spectrometer equipped with a specially designed high-pressure CI source operating in the temperature range 260–300 °C. *n*-Propyl phenyl ether (**1**) and its deuterated analogues **2**–**8** were prepared and purified by distillation as described previously.[7,8] Compound **9** was prepared by reducing dimethyl malonate with $LiAlD_4$, converting the resulting $HOCD_2CH_2CD_2OH$ into the ditosylate, reducing the latter with 1 equivalent of $LiAlH_4$ and displacing tosylate with NaOPh; after distillation, $PhOCD_2CH_2CD_2Cl$ was found to be the major impurity (presumably from formation of $ClCD_2CH_2CD_2OTs$ as a side product during the ditosylation step), but did not interfere with studies of metastable $MD^+$. The relative ion abundances appeared to vary with the amount of $D_2O$ in the ion source (since the MIKE spectra showed a decreasing extent of exchange of the CI hydron with the chain as more $D_2O$ was introduced), but reached a limiting value at the highest accessible partial pressures of $D_2O$. In the high pressure limit the BMIN experimental values for **1** and **2** are reproduced. Even at this high pressure limit, however, the metastable ion fragmentation pattern in the first field-free region (1st FFR) (examined by *B/E* scans) shows more exchange of the CI hydron with the chain does the fragmentation pattern the 2nd FFR (examined by MIKE spectrometry). Table 1 compares predictions made on the basis of the BMIN and two other purely statistical models with our MIKE results.

The BMIN model sets all isotope effects equal to unity and is summarized for **1** in Scheme 1. Deposition of $D^+$ on the ring leads to [cyclohexadienone isopropyl cation] complexes, in which proton transfer from the isopropyl cation to the oxygen yields fragment ions that contain one deuterium. There are three basic sites on the ring in addition to the basic oxygen. The BMIN model asserts that CI with a strong gaseous acid such as $D_3O^+$ will partition statistically among these four sites. Hence three-quarters of the fragment ions are proposed to result from direct ring deuteronation. Once the CI hydron is deposited on the ring, it does not exchange with the chain. By labeling experiments, Bogdanov *et al.*[6] demonstrated that the ring hydrogens are not involved in exchange or in transposition with the chain.

**Table 1. Predicted and experimental relative percentages of *m/z* 95:96:97 in the MIKE spectra (8.1 kV main beam) of *n*-propyl phenyl ether $MD^+$ ions from chemical ionization using $D_2O$ reagent gas**

| Parent neutral (M) | Predicted *m/z* 95:96:97 proportions for $MD^+$ | | | Observed *m/z* 95:96:97 |
|---|---|---|---|---|
| | BMIN | Modified BMIN | Randomized BMIN | |
| $PhOCH_2CH_2CH_3$ (**1**) | 10:90:0 | 18:82:0 | 19:81:0 | 9:91:0 |
| $PhOCH_2CD_2CH_3$ (**2**) | 7:78:15 | 12:74:14 | 9:67:24 | 6:79:15 |
| $PhOCD_2CH_2CD_3$ (**3**) | 0:18:82 | 0:20:80 | 0.8:32:67 | ⩽0.1:25:75 |
| $PhOCD_2CH_2CH_3$ (**4**) | 4:65:31 | 7:64:29 | 9:67:24 | 5:75:20 |
| $PhOCH_2CH_2CHD_2$ (**5**) | 4:65:31 | 7:64:29 | 9:67:24 | 9:70:21 |
| $PhOCD_2CD_2CH_3$ (**6**) | 2:51:47 | 4:52:45 | 3:46:52 | 4:60:37 |
| $PhOCH_2CH_2CD_3$ (**7**) | 2:51:47 | 4:52:45 | 5:57:38 | 5:58:38 |
| $PhOCH_2CD_2CH_2D$ (**8**) | 4:65:31 | 7:64:29 | 5:57:38 | 5:69:27 |
| $PhOCD_2CH_2CHD_2$ (**9**) | 0.7:35:64 | 1:37:62 | 9:67:24 | 1.5:45:53 |

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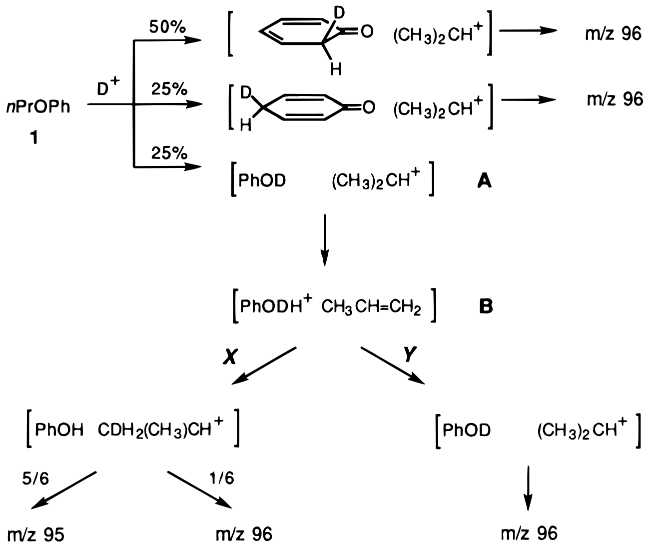

**Scheme 1**

Deposition of D$^+$ on the oxygen of **1** gives a [PhOD (CH$_3$)$_2$CH$^+$] complex, **A**, which undergoes internal proton transfer to isomerize to a [PhODH$^+$ propene] complex, **B**. Complex **B** then transfers a hydron back to the alkene to give two complexes (one of which appears to be indistinguishable from **A**) in proportions $X$ and $Y$. In the BMIN model $X$ and $Y$ are both equal to 0.5. We consider here two variations as well: (i) a modified BMIN model, in which the mole fractions $X$ and $Y$ represent the statistical proportions in the limit of complete equilibration, and (ii) the same modified BMIN model where, in addition, hydrogens randomize completely within the isopropyl cations in all of the complexes. For the modified BMIN model the proportions of $X$ and $Y$ in Scheme 1 become 6:7 and 1:7, respectively (instead of 1:2 and 1:2). For the randomized BMIN model $X$ and $Y$ are 7:8 and 1:8, respectively; in MD$^+$ ions from **2**–**9**, this model supposes that the isotope randomizes within the isopropyl cations of the [cyclohexadienone isopropyl cation] complexes as well as in the complexes analogous to **A**.

Examination of Table 1 shows that, despite the excellent agreement between the BMIN predictions and experiment for **1** and **2**, the agreement of any of the three purely statistical models with the experimental results for **3**–**9** is poor. Let us see if the BMIN model can be improved by allowing the mole fraction of *O*-deuteronation to have a value $Z$ and the mole fraction of ring deuteronation to be $1 - Z$, with an isotope effect $k_H/k_D$ in the final steps of Scheme 1. Letting $X = Y = 0.5$ these modifications give $m/z$ $96:95 = [2 + (10 - 5Z)k_H/k_D]/(5Zk_H/k_D)$ for the MD$^+$ ions of **1** and $m/z$ $97:96 = (60 - 5Z)/(5Z + 12k_H/k_D)$ for the MD$^+$ ions of **3**. For **3** the experimental values of the ratio are 3.0 (standard deviation (s.d.) = 0.1) and 2.9 (s.d. = 0.2) in two independent trials. Solving the algebra for these two compounds gives a ratio of ring to *O*-deuteronation $(1 - Z)/Z = 15$ and an isotope effect $k_H/k_D = 1.6$. However, application of those derived values to compound **2** predicts a fraction of $m/z$ 95 from its MD$^+$ ions of only 2%, at variance with the BMIN experimental value (and reproduced by us). Similarly, this expedient does not bring the model into line with the other experimental values.

The BMIN and modified BMIN models both predict that the tridenterated-compound **6** and the tetradeuterated-compound **7** should yield the same fragment ion distributions. While **6** and **7** do appear to give the same $m/z$ 95:96:97 ratios (within our experimental error), the proportions do not agree quantitatively with the predictions. Moreover, all three models predict that the two dideuterated-compounds **4** and **5** ought to yield identical distributions, which experiment does not bear out. The $m/z$ 96:97 ratio for **4** was measured as 4.1 (s.d. = 0.2) and 3.8 (s.d. = 0.3) in two independent trials, and that for **5** was measured as 3.15 (s.d. = 0.05) and 3.4 (s.d. = 0.1) in two independent trials. The introduction of further isotope effects might bring some of the predicted relative ion abundances into agreement with experiment, but could not account for the differences between **4** and **5**.

We have previously observed different product distributions in the molecular ions of **4** and **5** produced by photoionization.[8] In that case we inferred that this reflects the intermediacy of complexes containing corner-protonated cyclopropanes. Given the data at hand, it seems hard to avoid drawing a similar conclusion from the CI MIKE results. Moreover, the partitioning among sites where the CI hydron is deposited should not be taken to be statistical, but must be determined by experiment.

Additional, plausible variations to Scheme 1 would portray the arrows corresponding to $X$ and $Y$ as reversible, where return to **B** competes with the formation of $m/z$ 95 and 96 ions. In its general form, such a mechanism would also have to include features that we have previously discussed: a competing process by which deuterium transposes to C-2 of the isopropyl cation, as well as isotope effects.[4] Finally, the contribution from complexes containing protonated cyclopropanes ought not to be neglected.

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*Yours,*

JEAN-PAUL JACQUET[1] and THOMAS HELLMAN MORTON[1,2]
[1] DCMR, Ecole Polytechnique, 91128 Palaiseau, France
[2] Department of Chemistry, University of California, Riverside, California 92521-0403, USA

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