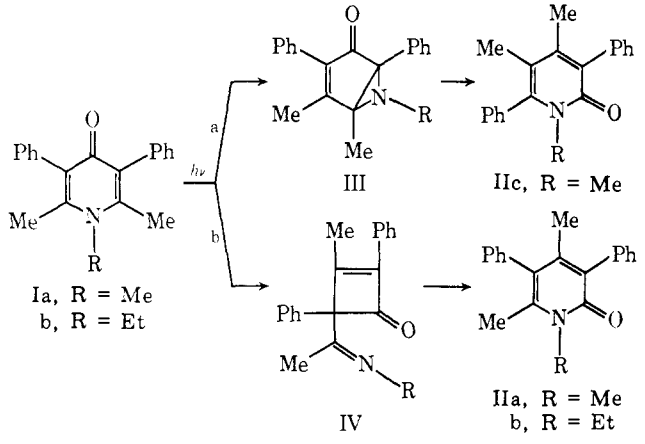
photolysis of 2,6-dimethyl-3,5-diphenyl-4-pyrone afforded 3,6-diphenyl-4,5-dimethyl-2-pyrone as the sole product.[8] Neither IIa nor IIc is a precursor for the other in the formation of IIc or IIa, independent thermolysis and irradiation of IIa or IIc having no effect. These results suggest the predominance of a distinctly different mechanism for the rearrangement of hindered 4-pyridones.

A tentative mechanism to account for the formation of 2-pyridones (II) from 4-pyridones (I) is presented in Scheme I. We believe that photolysis of the hindered

Scheme I



4-pyridones leads initially to the 6-azabicyclo[3.1.0]-hexenone (III)[16] which is converted, in either a photochemical or thermal process, to the pyridone IIc as a minor product (path a). This photoconversion is analogous to photoisomerization of the hindered 4- to 2-pyrones.[9] For the formation of the major product, photolysis of I may initially proceed by isomerization to the cyclobutenone derivative IV,[17] which is converted to II (path b). The entirely different nature of the photochemical primary reactions of furans and pyrroles was recently demonstrated by trapping of the transient species.[18,19] Stability of Id and Ie against light might be explained in terms of the steric effect of the substituents,[20] since molecular models show that C–N bond cleavage in Id and Ie would lead to the formation of intermediate III or IV in which there was appreciable steric hindrance.

The proposed mechanism, while it rationalizes the experimental observation presented, may not constitute a unique explanation for the results. An investigation of the factors influencing reactivity in the 4-pyridones is currently in progress.

Acknowledgments. We are grateful for Professor F. Mashio of this department for his encouragement during the course of this work.

(16) The synthetic method of the 6-azabicyclo[3.1.0]hexenyl system was recently reported: L. Kaplan, J. W. Pavlik, and K. E. Wilzbach, *J. Amer. Chem. Soc.*, **94**, 3283 (1972); A. Mishra, S. N. Rice, and W. Lwowski, *J. Org. Chem.*, **33**, 481 (1968).

(17) An isolation of vinylcyclobutenone from photolysis of 4-hydroxy-2,4,6-tri-*tert*-butylcyclohexa-2,5-dienone was reported: D. A. Plank, J. C. Floyd, and W. H. Starnes, Jr., *Chem. Commun.*, 1003 (1969).

(18) H. Hiraoka, *ibid.*, 1610 (1971).

(19) A preliminary attempt to trap the intermediate III or IV by methanol was unsuccessful and photolysis of Ia in methanol gave only IIa and IIc.

(20) Comparison of the absorption and emission (fluorescence and phosphorescence) spectra of Id and Ie with those of Ia and Ib did not give distinct evidence to distinguish their photoreactivity. Analysis of the absorption and emission spectra of 4-pyridones, 4-thiopyrones, and 4-pyrones will be published elsewhere.

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Gas-Phase Isopropylation of Toluene. On the Question of the Positional Selectivity in Gas-Phase Aromatic Substitutions

Sir:

From experiments carried out during the past five years in this laboratory with different gaseous electrophiles, including HeT^+ ions from the β decay of molecular tritium,[1-3] $^{80}Br^+$ ions from the isomeric transition of CH_3–^{80m}Br,[4] and radiolytically formed D_2T^+ [5] and alkyl[6] ions, we conclude that the gas-phase electrophilic attack on the aromatic ring is characterized by a significant *positional* selectivity.

In a recent paper the isomeric distribution of isopropyltoluenes from the gas-phase attack of radiolytically formed i-$C_3H_7^+$ ions on C_7H_8 was reported to be *statistical* (*i.e.*, 44.2% ortho, 40.4% meta, and 15.4% para) at low pressures of toluene, going to a *thermodynamically controlled* distribution (*i.e.*, 28.2% ortho, 59.2% meta, and 12.6% para) at higher pressures of toluene.

The formation of large amounts of the meta isomer was regarded as a typical feature of the gas-phase isopropylation, and the *statistical* distribution observed at low C_7H_8 pressures was ascribed to the inherent lack of selectivity of the gaseous i-$C_3H_7^+$ cation.

Since the behavior of the i-$C_3H_7^+$ ion described in ref 7 represented a conspicuous and disturbing departure from the selectivity established for other gaseous electrophiles, further investigation was undertaken in the hope of accounting for the discrepancy.

The isopropylation described in ref 7 was carried out with gaseous i-$C_3H_7^+$ ions obtained according to a general technique introduced by Ausloos and coworkers,[8] based on the γ radiolysis of a gaseous alkane, in this case C_3H_8, containing a radical scavanger and a low concentration of the aromatic substrate.

The well established radiation-induced decomposition of C_3H_8 and the subsequent ion–molecule reactions

$$C_3H_8 \rightsquigarrow C_3H_7^+ + H + e \quad (1)$$

$$C_3H_8 \longrightarrow C_2H_5^+ + CH_3 + e \quad (2)$$

$$C_2H_5^+ + C_3H_8 \longrightarrow C_2H_6 + C_3H_7^+, \text{ etc.} \quad (3)$$

of the charged fragments lead to the predominant formation of the secondary propyl ion, whose attack on toluene gives isomeric arenonium ions and eventually the isomeric isopropyltoluenes, following the loss of a

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(2) F. Cacace and G. Perez, *J. Chem. Soc. B*, 2086 (1971).
(3) F. Cacace, R. Cipollini, and G. Ciranni, *ibid.*, 2089 (1971).
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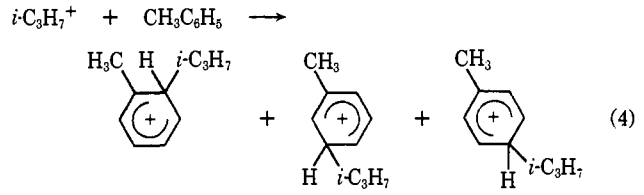
(6) F. Cacace, *et al.*, unpublished data.
(7) S. Takamuku, K. Iseda, and H. Sakurai, *J. Amer. Chem. Soc.*, **93**, 2420 (1971).
(8) For an exhaustive review, *cf.* P. Ausloos, "Ion-Molecule Reactions," J. L. Franklin, Ed., Plenum Press, New York, N. Y., 1970.

Table I. Dependence of the Products Composition on the Reaction Conditions

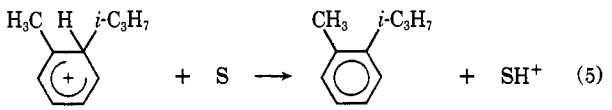
System composition				Isopropyltoluenes[a] (% rel yields)				
C_7H_8 (Torr)	C_3H_8 (Torr)	Base (Torr)	Dose, eV g^{-1}	Ortho	Meta	Para	Para:½ meta ratio	Ref
1.8	100	Unknown[b]	9.5×10^{20}	44.2	40.4	15.4	0.76	7
1.8	100[c]	EtOH, 8.0	9.5×10^{20}	49.1	32.5	18.3	1.13	This work
1.1	730[c]	EtOH, 4.1	6.2×10^{20}	43.6	31.7	24.6	1.55	This work
2.1	730[c]	EtOH, 6.0	3.7×10^{19}	42.3	33.2	24.5	1.48	This work
1.3	730[c]	EtOH, 22.6	1.2×10^{20}	35.5	27.2	37.2	2.70	This work

[a] The *absolute* yields varied with the composition of the system, as indicated by G values ranging from *ca.* 0.3 to *ca.* 0.09. The highest yield was obtained, as expected, at the highest (*ca.* 1:3) C_7H_8:C_2H_5OH molar ratio and is wholly consistent with those reported in ref 7, once the competition of ethanol for the i-$C_3H_7^+$ reagent is taken into account. The competition of the base explains also the observed decrease of the *absolute* yields at higher base(s) concentrations. [b] See ref 9. [c] The system contained O_2 (2 Torr) as a radical scavanger and was irradiated at the specified dose in a 5000-Ci Gammacell. The analysis of the products was carried out by glc using essentially the same columns as described in ref 7.



(4)

proton to a base contained in the system, *e.g.*



(5)

Inspection of the experimental conditions described in ref 7, *i.e.*, the relatively low pressure of C_3H_8 (100 Torr), the relatively high (1:20 to 1:10) C_7H_8 to C_3H_8 ratio, and the lack of a base[9] in the gaseous system, suggested that the "anomalous" selectivity reported for the gas-phase isopropylation might be traced to secondary isomerization of the protonated intermediates, an annoying side reaction long recognized in the study of liquid-phase Friedel–Crafts alkylations.[10]

The problem concerning how faithfully the isomeric composition of the products reproduces the ratio of the intermediate arenonium ions formed in the kinetically significant step of the reaction appears even more vexing in the gas phase and requires careful evaluation when the positional selectivity of a gaseous electrophile is deduced from the analysis of the final products. In fact, the generally large exothermicity of the attack by gaseous, unsolvated cations leads to the formation of excited arenonium ions that are likely to undergo intramolecular and/or intermolecular isomerization during their relatively long lifetime, before quenching *via* reaction 5 can occur. In order to ascertain whether or not secondary isomerization was taking place, the dependence of product composition on the conditions of the gas-phase isopropylation was investigated.

Some data of particular interest in connection with the problem of the *positional* selectivity of the gaseous i-$C_3H_7^+$ ion are compared in Table I with those reported in ref 7.

(9) No base was deliberately added to C_3H_8 in the experiments described in ref 7, and therefore no information on the nature and the concentration of the base(s) contained in the gaseous system is available. However, the formation of bases (propylene, water, alcohols, etc.) in unspecified concentrations during the radiolysis of C_3H_8 in the presence of O_2 was postulated to account for the occurrence of processes similar to reaction 5.

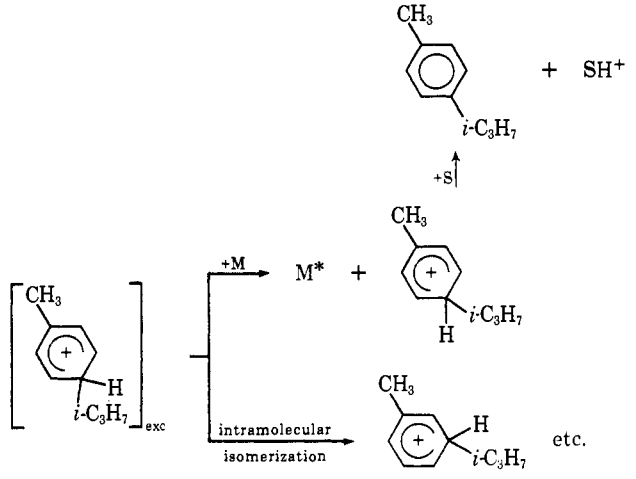
(10) *Cf.* "Friedel-Crafts and Related Reactions," G. Olah, Ed., Interscience, New York, N. Y., 1964.

The results show that, while insensitive to a 20-fold change of the radiation dose, the *apparent* positional selectivity of the gaseous i-$C_3H_7^+$ cation, as measured by the para:½ meta ratio of the isopropyltoluenes formed, markedly depends on the pressure of C_3H_8, the bulk constituent of the gaseous system, and, at a given pressure, on the concentration of the base contained in the gas.

At higher C_3H_8 and base pressures, the i-$C_3H_7^+$ ion *does indeed exhibit a positional selectivity*, fully comparable with those of other gaseous electrophiles, as indicated by a para:½ meta ratio in excess of 2.7.

These findings can be rationalized by taking into account the effects of C_3H_8 and base concentrations on the course of the competitive reaction pathways which eventually determine the composition of products, *e.g.*, Scheme I.

Scheme I



Higher C_3H_8 pressures enhance the efficiency of collisional stabilization, thus reducing the fraction of primary arenonium ions sufficiently excited to undergo isomerization before their quenching by the base. On the other hand, higher concentrations of the base reduce the lifetime of the arenonium ions, thus decreasing the time allowed for their intramolecular isomerization.

Finally, intermolecular isomerization, *i.e.*, C_7H_8 alkylation by primary arenonium ions, is also expected to be prevented by a sufficient concentration of the base.

We conclude that the gas-phase electrophilic attack of i-$C_3H_7^+$ on toluene is characterized, in analogy with the other gas-phase aromatic substitutions so far investigated, by a significant positional selectivity that

can only be measured when extensive isomerization of the arenonium ions formed in the kinetically significant step of the attack is prevented by a suitable choice of the reaction conditions.

It cannot be claimed that the present data fully reflect the inherent positional selectivity of gaseous *i*-$C_3H_7^+$, since, even under conditions specifically chosen to minimize secondary isomerization, its occurrence cannot be entirely excluded.

However, we feel that even the lower selectivity limit established in the present study, together with the results of previous investigations, indicates that the lack of positional selectivity *is not* a distinctive feature of the gas-phase alkylation and that the *i*-$C_3H_7^+$ cation represents no exception when compared to other gaseous electrophiles.

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Structure of A204A, a New Polyether Antibiotic

Sir:

Antibiotic A204A is the major factor of a group of closely related, biologically active compounds produced by a strain of *Streptomyces albus*.[1] It is active against Gram-positive bacteria, fungi, and several plant pathogens, and it is effective in the treatment of coccidial infections in poultry. In addition, A204A induces monovalent cation permeability in rat liver mitochondria.[2] In light of its biological activity and its physical properties, which are outlined below, A204A was thought to belong to the family of polycyclic, polyether, monocarboxylic acid antibiotics, which includes monensin,[3] nigericin,[4] X-537A,[5] grisorixin,[6] dianemycin,[7] and X-206.[8]

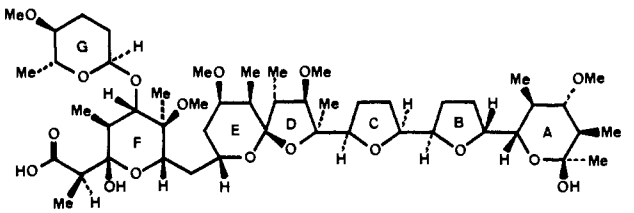
A204A is a monocarboxylic acid: mp 96–98°; pK_a' = 6.1 (66% DMF); $[\alpha]^{25}D$ +68.1° (*c* 2, MeOH); ν_{max} ($CHCl_3$) 1681 cm^{-1} (CO_2H); no uv maximum beyond 210 nm. The sodium salt of A204A (mp 144–145°; $[\alpha]^{25}D$ +55.0° (*c* 2, MeOH); ν_{max} ($CHCl_3$) 1600 cm^{-1} (CO_2^-)) and the free acid are insoluble in water but soluble in organic solvents. The nmr spectrum ($CDCl_3$) showed the presence of five methoxyl groups at δ 3.30–3.43, a number of *C*-methyl groups and protons attached to carbon atoms bearing oxygen, and a broad singlet at δ 4.85.

The silver and sodium salts of A204A crystallize from acetone–water as colorless, triangular plates which contain one molecule of acetone per molecule of antibiotic. The crystal data for the two nearly isomorphous salts are given in Table I. A total of 2409 unique reflections for the silver salt and 2457 for the sodium salt were measured using an automated diffractometer with filtered copper radiation. The structure of the silver salt was solved by the heavy atom technique, albeit with great difficulty because of the persistent pseudosymmetry. The structure of the silver salt has been refined to an *R* value of 0.15 by least-squares methods using anisotropic temperature factors for the heavy atom and isotropic factors for all other atoms. The structure of the sodium salt was refined using anisotopic temperature factors for the sodium and oxygen atoms to give an *R* value of 0.14. Further refinement has been hampered by the limited data available and by the apparent disorder of the acetone solvate molecule. The atomic parameters for the two salts are given in Table II, with the atoms numbered as in Figure 1.[9] The absolute configuration of the molecule was determined for the silver salt by anomalous dispersion.

Table I. Crystal Data for Silver and Sodium Salts of A204A, $C_{49}H_{83}O_{17}\cdot M\cdot C_3H_6O$

	M	
	Ag	Na
a	26.971 (4) Å	27.539 (4) Å
b	14.517 (2) Å	14.515 (2) Å
c	14.419 (2) Å	14.406 (2) Å
β	91.94 (1)°	92.36 (1°)
Space group	*C*2	*C*2
Molecules/cell	4	4
Obsd density	1.293 g cm^{-3}	1.190 g cm^{-3}
Obsd mol wt	1099	1031
Calcd mol wt	1110	1025

The free acid form (**1**) of A204A has the empirical



1

formula $C_{49}H_{84}O_{17}$ (mol wt 945.2), making it the largest of the known, naturally occurring, polyether antibiotics. The compound is a monocarboxylic acid, and, like nigericin, grisorixin, and dianemycin, it has a 30-carbon backbone. Rings A–F are very similar in structure and stereochemistry to nigericin and grisorixin, and ring G occurs identically in dianemycin.

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(8) J. F. Blount and J. W. Westley, *Chem. Commun.*, 927 (1971).
(9) A list of the atomic parameters (Table II) will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JACS-73-3399.