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Gas-Phase Cationic Benzoylation of Ambident Aromatic Substrates Studied with the Decay Technique

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Abstract: The gas-phase benzoylation of typical ambident aromatic substrates PhY (Y = OH, OMe, and NH_2) has been investigated by a combination of the decay technique and of FT ICR mass spectrometry. Labeled phenylium ions, $C_6X_5^+$ (X = H and T), from the decay of multiply tritiated benzene, C_6X_6, have been allowed to react with excess CO-containing traces of PhY (Y = OH, OMe, and NH_2), in the pressure range from 90 to 650 torr. Radio GLC and HPLC of the tritiated products demonstrate two competitive reaction channels, i.e., phenylation and benzoylation of the aromatic substrates. The results indicate a sharp kinetic bias of the gaseous phenylium ions for the aromatic substrates, measured by an apparent k_{CO}/k_{PhY} ratio of 0.12 (Y = OH), 0.13 (Y = OMe), and 0.04 (Y = NH_2) in the systems at nearly atmospheric pressure. Gas-phase benzoylation displays a high intramolecular selectivity, occurring exclusively at the *n*-type center of PhOH and $PhNH_2$. In the case of PhOMe, appreciable ring benzoylation is observed, characterized by a remarkably high (up to 30:1) bias for the para position. The mechanistic features of the gas-phase benzoylation and phenylation processes, deduced from the decay and the ICR experiments, are discussed and compared with those of related aromatic acylation and alkylation reactions occurring in the dilute gas state.

The study of gas-phase aromatic substitution by charged electrophiles has greatly benefited by the combination of mass spectrometry, which permits direct detection of the ionic intermediates, with techniques which allow the determination of the isomeric composition of the products. Among the latter approaches, the decay technique, which utilizes the spontaneous β decay of covalently bound tritium atoms as a source of cations of known structure, has gained recognition as a powerful, if experimentally demanding, mechanistic tool.[1]

This work represents a continuation of studies on the gas-phase reactivity of free phenylium ions toward π-type and *n*-type nucleophiles, carried out in our laboratories with a combination of ICR mass spectrometry and the decay technique.[2-7] In particular, a preliminary investigation has shown that gaseous benzoyl cations can be obtained from the attack of decay phenylium ions on carbon monoxide.[3] We report here the results of a study of aromatic benzoylation in the dilute gas state.

Experimental Section

Materials. The preparation, purification, and isotopic analysis of multitritiated benzene, used as a source of the labeled decay ions, have been described elsewhere.[8,9] The compounds used as substrates, or as reference standards, in GLC and HPLC were research-grade chemicals from commercial sources, purified by preparative GLC and identified by NMR techniques. The gases (CO, O_2, and NMe_3) were research-grade samples from Matheson Gas Products Inc.

Preparation of the Decay Samples. Multitritiated benzene (1.0–1.4 mCi), diluted with C_6H_6 to a specific activity of ca. 100 mCi mmol^{-1}, was introduced by conventional vacuum techniques into evacuated and carefully outgassed Pyrex vessels (500–1000 mL), together with small amounts (5–10 torr) of the aromatic substrates and excess CO (90–630 torr). All systems contained O_2 as a radical scavenger, and a gaseous base (NMe_3, ca. 10 torr) was added when required. The vessels were sealed off and stored in the dark at 100 °C for periods of 15–20 months.

Analysis of the Radioactive Products. The products, extracted with ethyl acetate, were analyzed by radio GLC and HPLC. The absolute yields were calculated from the ratio of the activity found in each product to the total activity of the labeled decay ions formed in the system, which was deduced from the initial activity of multitritiated benzene, its isotopic composition, the known decay rate of tritium, and the storage time. The radioactive products from phenol and anisole were analyzed by radio GLC, using a Model 4200 instrument from C. Erba Co., equipped with a hot-wire detector in series with a 10-mL internal-flow proportional counter, Model LP 2007 M from Berthold Laboratorium AG. Helium, used as the carrier gas, was diluted with methane in order to obtain a 1:1 mixture suitable as the counting gas for the proportional tube, operated at 120 °C. The following columns were used: (i) GAL, 20% w/w on Chromosorb W, 2 m, 150 °C; (ii) SP-1200, 20% + Bentone 34, 3%, on Chromosorb W, 2 m, 140 °C. The products from aniline were analyzed by radio HPLC, using a Series 3B chromatograph from Perkin-Elmer Co., equipped with a Packard Tricarb RAM 7500 flow radioactivity monitor. The separation was carried out with a 5μ-Spherisorb ODS column (150 × 4 mm) using a mixture of phosphate buffer (pH 3) and methanol as the mobile phase, in the initial ratio 55:45 (v/v), linearly brought to 30:70 in 20 min, at a total flow rate of 1.0 mL min^{-1}.

Fourier Transform (FT-ICR) Mass Spectrometry. The measurements were performed with a Nicolet FT-MS 1000 ICR spectrometer, equipped with a 2.54-cm cubic cell installed between the poles of a 2.0-T superconducting magnet. The pressure measurements (uncorrected) were obtained with a Granville-Phillips 280 Bayard-Alpert ion gauge. Resolution was typically 1000 fwhh (full width half height) at *m/e* 100. The inlet system and the trapping cell were kept at room temperature, the ions being trapped within the cell by a differential voltage of ca. 1.0 V. Typical operating conditions were as follows: nominal electron energy, 15 eV, electron beam pulse time, 3 ms, emission current, 0.400 μA, total pressure from 2 to 5 × 10^{-6} torr. The benzoyl cation, conveniently formed by electron impact on PhCHO, was isolated from other ions by the triple-resonance technique, and its reactions with aromatic substrates were monitored by analyzing any daughter cations formed.

Results

The yields of the labeled products from the decay of multitritiated benzene, C_6X_6 (X = H, T), in gaseous CO containing minor amounts of phenol and/or anisole are given in Table I and those from the systems containing aniline in Table II. In the absence of other nucleophiles, the combined yields of the aromatic products identified range from 65 to 76% of the activity of the $C_6X_5^+$ decay ions formed in the system, which represents the maximum activity theoretically incorporable in the products. Such a high recovery

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(1) (a) Cacace, F. *Adv. Phys. Org. Chem.* **1970**, *8*, 79. (b) Cacace, F. In "Kinetics of Ion-Molecule Reactions"; Ausloos, P., Ed.; Plenum Press: New York, 1979. (c) Speranza, M. *Gazz. Chim. Ital.* **1983**, *113*, 37.

(2) Angelini, G.; Fornarini, S.; Speranza, M. *J. Am. Chem. Soc.* **1982**, *104*, 4773.

(3) (a) Occhiucci, G.; Patacchiola, A.; Sparapani, C.; Speranza, M. *J. Chem. Soc., Chem. Commun.* **1982**, 1269. (b) Occhiucci, G.; Speranza, M.; Cacace, F. *J. Chem. Soc. Chem. Commun.* **1984**, 723.

(4) Fornarini, S.; Speranza, M. *J. Chem. Soc., Perkin Trans. 2* **1984**, 171.

(5) Speranza, M.; Keheyan, Y.; Angelini, G. *J. Am. Chem. Soc.* **1983**, *105*, 6377.

(6) Angelini, G.; Sparapani, C.; Speranza, M. *Tetrahedron* **1984**, *40*, 4865.

(7) Colosimo, M.; Speranza, M.; Cacace, F.; Ciranni, G. *Tetrahedron* **1984**, *40*, 4873.

(8) Angelini, G.; Speranza, M.; Segre, A. L.; Altman, L. J. *J. Org. Chem.* **1980**, *45*, 3291.

(9) Cacace, F.; Speranza, M.; Wolf, A. P.; Ehrenkaufer, R. *J. Labelled Compds. Radiopharm.* **1982**, *19*, 905.

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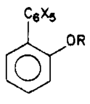
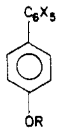
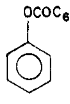
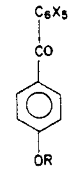
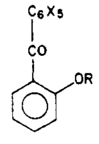
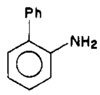
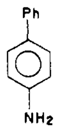
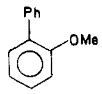
Table I. Decay of Multitritiated Benzene in Excess CO-Containing Phenol and Anisole

system comp,[a] torr				rel activity of labeled products,[b] %						
CO	PhOH	PhOMe	NMe_3	$PhOC_6X_5$						overall abs yield,[c] %
88	5.7			21.3	13.2[d]		65.5			72
628	11.5			5.0	7.5[d]		87.5			68
615	11.0		12.5	19.7	11.2[d]		69.1			19
634	11.0	11.8	12.6	22.8	6.5[d]		41.3			36
					18.2[e]	11.2[e]				
88		5.8		12.6	12.3[e]	10.5[e]	19.3	43.8[e]	1.4[e]	76
628		11.1		4.5	7.8[e]	5.1[e]	5.7	71.6[e]	5.2[e]	65
628		12.1	12.6	24.1	32.4[e]	19.1[e]	24.4			29

[a] All systems contained C_6X_6 (X = H and T), 0.8–1.5 mCi, and O_2 (ca. 5 torr) as a radical scavenger. [b] Standard deviation of the data ca. 10%. [c] Standard deviation of the data ca. 20%; detection limit of the products ca. 1% absolute yield. [d] R = H. [e] R = Me.

Table II. Decay of Multitritiated Benzene in Excess CO-Containing Aniline and Anisole

system comp,[a] torr				rel activity of labeled products,[b] %					
CO	$PhNH_2$	PhOMe	NMe_3	PhCONHPh	Ph_2NH				overall abs yield,[c] %
87	5.9			68.5	12.5	14.0	5.0		70
636	8.6			76.8	7.7	9.7	5.8		54
636	10.3		12.5	79.2	20.8				12
636	11.4	13.0	12.5	89.5	10.5				22
636	11.5	9.0		64.6	4.4	6.6	4.4	20.0	50

[a] All systems contained C_6X_6 (X = H and T), 0.8–1.5 mCi, and O_2, 5 torr, as a radical scavenger. [b] Standard deviation ca. 10%. [c] Standard deviation ca. 20%; detection limit of the products, ca. 1% absolute yield.

demonstrates the ability of the radioanalytical procedures adopted to trace the major reaction channels of the charged electrophile. The sharp decrease of the absolute yields of aromatic products from the systems containing NMe_3 supports the ionic nature of the phenylation and benzoylation processes, since the amine is known to be an effective interceptor of gaseous cations.

The most significant features of the results can be summarized as follows.

(i) The *substrate* selectivity of gaseous phenylium ion is characterized by a sharp bias in favor of the aromatic substrates with respect to CO, the apparent k_{CO}/k_{PhY} ratios being as low as 0.12 (Y = OH), 0.13 (Y = OMe), and 0.04 (Y = NH_2) in systems at nearly atmospheric pressure.

(ii) The ionic phenylation shows an appreciable *positional* selectivity. Under the conditions most favorable to kinetic control of products, i.e., at the higher pressure and in the presence of NMe_3, phenol undergoes predominant O-phenylation, ring substitution occurring exclusively at the ortho positions. Anisole undergoes phenylation at the ortho and para positions, whose ratio in CO at 628 torr ranges from 1.5 to 1.7, depending on the composition of the system. Of special note is the formation of diphenyl ether, whose relative yield increases at low pressure and especially in the presence of NMe_3. Aniline undergoes exclusive N-phenylation in gaseous systems containing NMe_3, while in neat CO ring substitution takes place as well at the ortho and para positions, at a ratio ranging from 1.7 to 2.8, depending on the pressure. In view of the remarkable regioselectivity observed, it is tempting to envisage that the primary attack of the Ph^+ ion occurs at the *n*-type center of the aromatic substrate, followed by partial rearrangement into ring-phenylated adducts. A noteworthy feature is that under no circumstances, nor even at low pressure, does the highly exothermic ionic phenylation occur at the ring positions meta to the activating OH, OMe, and NH_2 substituents.

(iii) As can be expected owing to its milder character, $C_6X_5CO^+$ displays a much more pronounced selectivity than $C_6X_5^+$, leading to exclusive acylation of the *n*-type center of phenol and aniline. Only when O-substitution cannot lead to isolable neutral products, as in the case of anisole, does appreciable ring benzoylation occur, with a remarkable (up to 30:1) bias for the para position.

Discussion

Ionic Reagents. The formation of labeled phenylium ions from the decay of multitritiated benzene has been discussed in detail elsewhere.[2,4,10] The daughter ions **1** are formed in high (72%)

$$C_6X_6 \xrightarrow{\beta\text{ decay}} \underset{\mathbf{1^*}}{C_6X_5^+} + {}^3He + \beta^- \qquad (1)$$

yields,[11] in a vibrationally excited state, owing to the relaxation of their initially regular structure, reminiscent of the parent benzene, to the deformed ring typical of ground-state phenylium ion. The excess internal energy of **1***, ranging from 25 to 32 kcal mol^{-1} according to different calculations,[12] can affect the reactivity of the decay ions toward CO, while collisional deactivation is likely to thermalize the ionic species well before their reactive encounter with the aromatic substrates, highly diluted in carbon monoxide.

Formation of the benzoyl cation is traced to process 2 whose exothermicity is ca. 78 kcal mol^{-1}.[13] In agreement with previous

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(10) Speranza, M. *Tetrahedron Lett.* **1980**, *21*, 1983.

(11) Carlson, T. *J. Chem. Phys.* **1960**, *32*, 1234.

(12) The upper limit of such "deformation energy" is estimated from ca. 25 kcal mol^{-1} (cf.: (a) Dill, J. D.; Schleyer, P. v. R.; Binkley, J. S.; Seeger, R.; Pople, J. A.; Haselbach, E. *J. Am. Chem. Soc.* **1976**, *98*, 5428) and 32 kcal mol^{-1} (cf.: (b) Schleyer, P. v. R.; Kos, A. J.; Raghavachari, K. *J. Chem. Soc., Chem. Commun.* **1983**, 1296). The more recent value, 32 kcal mol^{-1}, appears the most reliable one.

(13) Heat of formation of gaseous $PhCO^+$ is 174.6 kcal mol^{-1} according to: (a) Davidson, W. R.; Meza-Hojer, S.; Kebarle, P. *Can. J. Chem.* **1979**, *57*, 3205. A slightly lower value is given by: (b) McLoughlin, R. G.; Traeger, J. C. *Org. Mass Spectrom.* **1979**, *14*, 434. The heat of formation of Ph^+ is 279 kcal mol^{-1} according to: (c) Lossing F. P.; Holmes, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 6917 and references therein. The data concerning neutral molecules are taken from: (d) Cox, J. D.; Pilcher, G. "Thermochemistry of Organic and Organo-metallic Compounds"; Academic Press: New York, 1970.

findings,[3a] it is apparent from Tables I and II that the yields of

$$C_6X_5^+ + CO \rightarrow \underset{\mathbf{2}}{C_6X_5CO^+} \qquad (2)$$

benzoylated products are much lower than expected from the [CO]/[PhY] ratios, if one assumes that the reactivity of gaseous phenylium ion **1** toward CO and the aromatic substrates is comparable.

Prima facie, the composition of the labeled products points to a significant selectivity of the phenylium ion, suggesting that its attack on the aromatic substrates is considerably faster than reaction 2. Such a sharp discrimination of a free, unsolvated,

$$\mathbf{1} + PhY \rightarrow [C_6X_5PhY]^+ \qquad (3)$$

and extremely reactive[14] gaseous cation between two comparably exothermic channels is of considerable mechanistic interest, and the matter deserves a brief discussion. In the first place, it is legitimate to inquiry whether the composition of the neutral products reflects indeed a kinetic bias of **1** in favor of the aromatic substrates, i.e., a high k_3/k_2 ratio, or alternative explanations are conceivable. Among the latter, the most obvious possibility is that only a small fraction of the benzoyl cations from (2) evolve into isolable neutral products. However, the overall *absolute* yields of the products, as high as 70%, definitely make such hypothesis untenable.

Another conceivable explanation is that the benzoyl cation from (2) can act in the gas phase as a phenylating, as well as an acylating, reagent undergoing the nucleophilic displacement

$$\mathbf{2} + PhY \rightarrow CO + [C_6X_5PhY]^+ \qquad (4)$$

In order to evaluate such possibility, specifically designed ICR experiments have been carried out, by allowing benzoyl cations obtained by electron impact on benzaldehyde to react with phenol and anisole at pressure ranging from 2 to 5 × 10^{-6} torr. Occurrence of reaction 4 could never be observed, despite the fact that unlike highly exothermic addition processes, moderately exothermic displacement reactions, such as (4), are generally well-detectable under typical ICR conditions.

As suggested in a previous report,[3a] still a further possibility does exist, namely that a large fraction of the excited adducts **2** undergoes reversible dissociation. Such interpretation deserves careful consideration, in view of the highly exothermic character of reaction 2 and of the lack of low-energy fragmentation channels of **2** other than the loss of CO. Nevertheless, the data of Tables I and II show that the apparent k_2/k_3 ratios actually *decrease* in passing from low-pressure (ca. 95 torr) to high-pressure (ca. 640 torr) systems, at least in those containing phenol and aniline. Furthermore, one should consider that the competing reactions 3 are *even more exothermic* (vide infra) than process 2. All considered, the extensive dissociation of **2** that would be required to justify the relatively low rate of benzoylation is very unlikely in gaseous systems at nearly atmospheric pressure.

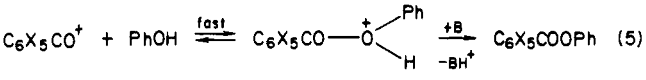
In the lack of plausible alternatives, one is forced to conclude that reaction 2 is *inherently slower* than aromatic phenylation (3) by at least an order of magnitude. In evaluating the factors that can account for the relative inefficiency of (2), it should preliminary be recognized that a purely physical interpretation is hardly satisfying. In fact, according to current models of ion–dipole interaction,[15] the smaller capture cross section of CO (μ = 0.12 D) than of the competing aromatic substrates, e.g., phenol (μ = 1.70 D), would be insufficient to quantitatively account for the observed selectivity of **1**, especially at the temperature (100 °C) of the decay systems. Another possibility is to attribute a sufficiently high activation energy to the attack of phenylium ion on the C atom of CO. A difficulty of this interpretation is that E_2^* should be unusually high, if one considers that the $C_6X_5^+$ ions from the decay of C_6X_6 possess a significant (25–32 kcal mol^{-1}) excess of internal energy. A more satisfactory explanation can proceed from the *kinetic* bias invariably displayed by gaseous carbonium ions, including Ph^+, for the *n*-type centers of ambident substrates.[16] This general trend suggests preferred phenylation of the O atom of CO, yielding **3** as the major primary adduct.

$$\underset{\mathbf{3}}{C_6X_5{}^+O{-}C} \qquad \underset{\mathbf{4}}{CH_3{-}CO^+} \qquad \underset{\mathbf{5}}{CH_3{-}{}^+OC}$$

While **3** has not been the subject of a specific theoretical analysis, ab initio calculations have been performed for the model acylium ion **4** and its isomer **5**, showing that the latter is less stable by some 50 kcal mol^{-1}, while the calculated barrier E_I^* for the isomerization **4** → **5** is very close (within a couple of kcal mol^{-1}) to the energy E_D required for the dissociation of **5** into CH_3^+ and CO.[17]

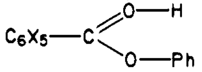
If one is willing to generalize these results, the relative inefficiency of reaction 2 can be rationalized by invoking the kinetically predominant formation of **3** from the attack of $C_6X_5^+$ on carbon monoxide. Isomerization to the benzoyl cation **2** would be allowed only to those ions that, sufficiently stabilized by collisional deactivation to escape dissociation back to $C_6X_5^+$ and CO, still retain sufficient internal energy to overcome the activation barrier E_I^*. The presumably narrow energy window leading to isomerization would then explain the inefficiency of the benzoylation channel. In fact, in contrast with the benzoyl cation **2**, the postulated adduct **3**, essentially a CO-solvated phenylium ion, is expected to readily undergo nucleophilic displacement of CO by the aromatic substrates, reacting as a phenylating agent. Perhaps it is worth mentioning that attack on the O atom of CO, followed by a 1,2-alkyl shift, has been considered as a plausible mechanism of the Koch reaction[18] and that charged intermediates analogous to **3** have been detected in the reaction of alkoxide and carbenes.[19]

Gas-Phase Aromatic Benzoylation. The results conform to a simple model, based on the assumption that the rate of attack on the O atom of phenol and anisole is much higher than of ring acylation. The exothermicity of addition 5 and therefore the ability of **6** to survive back dissociation are considered to be quite low. In fact, approximate calculations[20] show that an addition analogous to eq 5, but yielding instead the isomeric adduct protonated at the carbonyl oxygen, is exothermic by ca. 34 kcal mol^{-1}. Since the stability of **6** is *lower* than that of **7** by some 20–25 kcal mol^{-1}, according to PA correlations[21] and by analogy with similar isomeric pairs,[22] the view that **6** lies in a very shallow energy well,



$$C_6X_5CO^+ + PhOH \overset{fast}{\rightleftharpoons} C_6X_5CO{-}\overset{+}{O}\genfrac{}{}{0pt}{}{Ph}{H} \xrightarrow[-BH^+]{+B} C_6X_5COOPh \qquad (5)$$

6



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(14) Speranza, M.; Sefcik, M. D.; Henis, J. M. S.; Gaspar, P. P. *J. Am. Chem. Soc.* **1977**, *99*, 5583.

(15) All the experimental PA values are taken from: (a) Su, T.; Bowers, M. T. In "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 1, p 83. (b) Lias, S. G.; Liebman, J. F.; Levin, R. D. *J. Phys. Chem. Ref. Data* **1984**, *13*, 695.

(16) A kinetic bias for the *n*-type center has been observed in the gas-phase attack of gaseous cations, e.g. Et^+, i-Pr^+, t-Bu^+, Me_2F^+, Me_2Cl^+, and $MeCO^+$, on ambident substrates, e.g., phenol, anisole, halobenzenes, aniline, etc., cf. ref 1b, as well as: Cacace, F. *Radiat. Phys. Chem.* **1982**, *20*, 99. Concerning specifically phenylium ion, cf. ref 3, supported by the results of this study.

(17) Nobes, R. H.; Bouma, W. J.; Radom, L. *J. Am. Chem. Soc.* **1983**, *105*, 309.

(18) Hogeveen, H.; Roobeek, C. F. *Tetrahedron Lett.* **1971**, *36*, 3343.

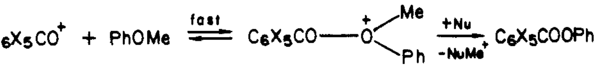
(19) Skell, P. S.; Starer, I. *J. Am. Chem. Soc.* **1959**, *81*, 4117.

(20) Based on a PA value of 212 kcal mol^{-1} of phenyl benzoate, calculated by using the correlation given by: Davis, D. W.; Rabelais, J. W. *J. Am. Chem. Soc.* **1974**, *96*, 5305.

(21) The PA of the singly bonded oxygen of phenyl benzoate can be estimated by using the correlation between the O(1s) ionization potential and the valence shell ionization potential given by Benoit and Harrison (Benoit, F. M.; Harrison, A. G. *J. Am. Chem. Soc.* **1977**, *99*, 3980) and the correlation between the valence shell ionization potential and the PA of the singly bonded oxygen given in ref 20.

and therefore is prone to back dissociation, seems amply justified. Deprotonation by a suitable gaseous base is the only channel available to prevent dissociation of **6** into PhOH and $PhCO^+$, especially since its isomerization into the more stable adduct **7** is believed to involve an appreciable activation energy.[13a] Since the PA of the singly bonded oxygen atom of phenyl benzoate is quite comparable to that of phenol, deprotonation of **6** can be carried out efficiently by the substrate itself, even in the gaseous sytems containing no NMe_3.

The adduct from the O-acylation of anisole obviously cannot evolve into neutral products via the relatively fast proton-transfer



$$C_6X_5CO^+ + PhOMe \overset{fast}{\rightleftharpoons} C_6X_5CO{-}\overset{+}{O}{<}^{Me}_{Ph} \xrightarrow[-NuMe^+]{+Nu} C_6X_5COOPh \quad (6)$$

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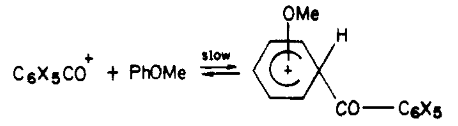
reactions accessible to **6**, requiring instead Me^+ removal by a suitable nucleophile, presumably a slow process in the systems containing no additives.

This accounts for the otherwise surprising increase of the *absolute* yields of C_6X_5COOPh in the presence of NMe_3, which is especially noteworthy if one considers that the amine intercepts a considerable fraction of the $C_6X_5^+$ and $C_6X_5CO^+$ precursors.

In neat CO, back dissociation of **8** predominates, allowing detection of the slower reaction channel ring substitution (7).



(7)

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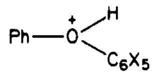
The isomeric acylated adducts **9** can in turn evolve into neutral products, i.e., isomeric methoxybenzophenones, via deprotonation by a gaseous base, possibly following intramolecular proton shifts of moderate activation energy,[23] which stabilize **9** against back dissociation.

When present, NMe_3 favors formation of C_6X_5COOPh, as shown in eq 6 and suppresses the slow ring substitution process (7) by intercepting the $C_6X_5CO^+$ cations.

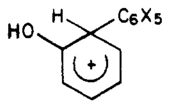
The results of this study characterize the gaseous benzoyl cation as a mild, selective electrophile, which displays a sharp kinetic bias for the *n*-type nucleophilic centers of the ambident substrates and, whenever ring substitution occurs, for the position para to the *n*-type activating group. The picture is consistent with earlier results, demonstrating the lack of reactivity of gaseous $PhCO^+$ toward π-type centers, even if strongly activated, as in C_6HMe_5,[3b] and with the behavior of gaseous acetylium ion. The latter displays a reactivity similar, if appreciably less selective, to the benzoyl cation, as could be expected from the lower extent of the charge delocalization in the smaller $MeCO^+$ ion. Thus, phenol undergoes acetylation predominantly (84%) at the oxygen atom, and attack of gaseous $MeCO^+$ on anisole yields 32% of the para-acetylated isomer.[24] In the same way, $PhCO^+$ attacks phenol exclusively at the *n* center, while anisole undergoes 93% benzoylation at the para position.

As to aniline, gas-phase ionic acetylation occurs almost exclusively (94%) at the N atom,[25] showing again a slightly lower selectivity than gaseous $PhCO^+$.

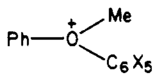
Phenylation Process. The presence of a large excess of carbon monoxide makes it difficult to assess whether the phenylation process is promoted by free $C_6X_5^+$ decay ions or by some weakly bound adduct, such as **3**, containing CO. Irrespective of the free or "solvated" nature of the electrophile, its attack can occur either on the *n*-type or on the π-type nucleophilic centers of the ambident substrates, e.g., phenol, yielding respectively oxonium or arenium ions.



10



11

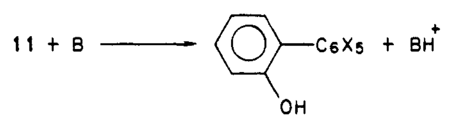


12

The reaction is undoubtedly exothermic, as shown by approximate calculations, leading to a $\Delta H°$ value of ca. −85 kcal mol^{-1} for the formation of **10** from PhOH and the free phenylium ion.[26] It is worth mentioning that unlike alkylation by Et^+, i-Pr^+, t-Bu^+, and other carbonium ions, phenylation is not complicated by simultaneous proton transfer from the electrophile to the substrate, since the PA of benzyne, the conjugate base of Ph^+, is *higher* than of PhOH, PhOMe, and even of $PhNH_2$.[27]

The adducts **10** and **11**, thermalyzed by unreactive collisions in the CO bath gas, yield, respectively, labeled diphenyl ether and 2-hydroxybiphenyl, following deprotonation.

$$\mathbf{10} + B \longrightarrow PhOC_6X_5 + BH^+ \quad (8a)$$

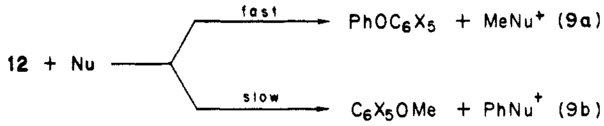


(8b)

In the absence of NMe_3, the strongest base present in the gas is PhOH, whose PA however is lower than that of Ph_2O.[28] As a consequence, deprotonation is relatively slow, requiring the cooperative interaction of at least two molecules of the base in a gaseous cluster. This consideration, and the possible occurrence of intermolecular Ph^+-transfer processes, suggests that the results most significant from the kinetic standpoint are those obtained in the presence of NMe_3, which ensures a fast deprotonation of **10** and **11** owing to its high PA.[15] Under these conditions, phenylation of PhOH displays a distinct bias for the oxygen atom, with an apparent k_0/k_{ring} ratio of ca. 1.8, comparable to the 2.1–2.4 ratios typical of gaseous cations, such as Me_2F^+ and Me_2Cl^+ which react exclusively as alkylating agents.[29]

Ring substitution of PhOH occurs exclusively at the ortho positions, which appears hard to reconcile with the extremely high reactivity and lack of selectivity of the free $C_6X_5^+$ ion, suggesting the intervention of a milder phenylating reagent, such as **3**.

Attack on the oxygen atom of PhOMe yields the oxonium ion **12**, which cannot evolve into neutral products via deprotonation, requiring instead Me^+, or Ph^+, transfer to a suitable nucleophile, i.e., anisole itself or, even better, NMe_3. The isolation of $PhOC_6X_5$, without appreciable formation of C_6X_5OMe, suggests that Me^+ transfer from **12** occurs at a significantly higher rate than Ph^+ transfer.



$$\mathbf{12} + Nu \xrightarrow{fast} PhOC_6X_5 + MeNu^+ \quad (9a)$$

$$\mathbf{12} + Nu \xrightarrow{slow} C_6X_5OMe + PhNu^+ \quad (9b)$$

As to aniline, the ratio of N-phenylated to ring-phenylated products is dramatically affected by the presence of NMe_3, as could be expected from the high PA of Ph_2NH, which requires intervention of a very strong base to ensure efficient deprotonation

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[22] The difference between the PA of the carbonyl oxygen atom and of the singly bonded oxygen atom of acetic acid is estimated to be 24 kcal mol^{-1}, ref 21. Similar conclusions have been reached in ref 13a.

[23] The activation energy for 1,2-proton shifts in arenium ions are in general much lower than the activation energy for processes analogous to **6** → **7** isomerization, cf.: Koptyug, V. A. In "Contemporary Problems in Carbonium Ions"; Rees, C., Ed.; Springer-Verlag: Berlin, 1984; Vol. 3, p 146.

[24] Giacomello, P.; Speranza, M. *J. Am. Chem. Soc.* **1977**, *99*, 7918.

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[26] Based on the heat of formation of Ph^+, ref 13c, and a PA of Ph_2O calculated according to the correlation given in ref 21.

[27] According to Pollack and Hehre ((a) Pollack, S. K.; Hehre, W. J. *Tetrahedron Lett.* **1980**, *21*, 2483) the PA of *o*-benzyne is ca. 213 kcal mol^{-1}, which exceeds those of PhOH, 197.5 kcal mol^{-1}, and anisole, 201 kcal mol^{-1}, according to Lau and Kebarle ((b) Lau, Y. K.; Kebarle, P. *J. Am. Chem. Soc.* **1976**, *98*, 7452) and that of aniline, 211.5 kcal mol^{-1} according to ref 15. All values adjusted to a reference value of 205 kcal mol^{-1} for the PA of NH_3.

[28] Cf. ref 26 and 27.

[29] Pepe, N.; Speranza, M. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1430.

of $C_6X_5{}^+NH_2Ph$, the adduct from attack on nitrogen. Under conditions favoring the kinetic control of product composition, i.e., in the presence of NMe_3 which ensures fast deprotonation of the primary intermediates, $PhNHC_6X_5$ is the only product observed. Taking into account the detection limit of the radiometric analysis, this corresponds to a k_N/k_{ring} ratio in excess of 10:1. Despite the uncertainty as to the free or CO-solvated nature of the phenylium ion in the present experiments, their result does not conflict with a previously established trend,[25] namely that the N-alkylating ability of carbenium ions in their reaction with gaseous aniline increases with the hardness of the cations.[30]

WARNING: The experiments reported involve the use of tritiated compounds of relatively high volatility, whose safe handling requires adequate confinement, e.g., a standard radiochemical hood.

Acknowledgments. Work was carried out with the financial support of the Italian National Research Council (C.N.R.) and of the Ministero della Pubblica Istruzione. We acknowledge the collaboration of Aldo Patacchiola and Dr. Roberto Gabrielli of the Servizio FT-MS of the Area della Ricerca C.N.R., Roma.

Registry No. C_6X_6 (X = H and T), 13967-78-7; PhOH, 108-95-2; PhOMe, 100-66-3; $PhNH_2$, 62-53-3; CO, 630-08-0; $PhOC_6X_5$ (X = H and T), 99747-37-2; HO-*o*-$C_6H_4C_6X_5$ (X = H and T), 99747-38-3; MeO-*o*-$C_6H_4C_6X_5$ (X = H and T), 99747-39-4; MeO-*p*-$C_6H_4C_6X_5$ (X = H and T), 99747-40-7; $PhOCOC_6X_5$ (X = H and T), 99747-41-8; MeO-*p*-$C_6H_4COC_6X_5$ (X = H and T), 99747-42-9; MeO-*o*-$C_6H_4COC_6X_5$ (X = H and T), 99747-43-0; PhCONHPh, 93-98-1; Ph_2NH, 122-39-4; Ph-*o*-$C_6H_4NH_2$, 90-41-5; Ph-*p*-$C_6H_4NH_2$, 92-67-1; Ph-*o*-C_6H_4OMe, 86-26-0.

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[30] For instance, the k_N/k_{ring} ratio in the gas-phase *tert*-butylation of aniline is 6.2, cf. ref 25.

The Microwave Spectra, Electric Dipole Moment, and Molecular Structure of *trans*-1,2-Difluorocyclopropane

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Abstract: The microwave spectra of *trans*-1,2-difluorocyclopropane were assigned and fitted to a first-order centrifugal distortion model. Microwave transitions of seven deuterium and carbon-13 isotopomers were observed and used to obtain a complete molecular structure. The partial Kraitchman parameters are $r(C_{1,2}–C_3)$ = 1.488 (5), $r(C_1–C_2)$ = 1.466 (4), r(C–F) = 1.383 (3), $r(C_1–H)$ = 1.090 (4), and $r(C_3–H)$ = 1.083 (2) Å and θ(HCF) = 111.3 (4) and θ(HCH) = 116.8 (2)°. The electric dipole moment, which is along the 2-fold symmetry axis, was measured to be 1.18 (1) D. All ring bonds in *trans*-1,2-difluorocyclopropane are shorter than the C–C bonds in cyclopropane. However, the orientation of the HCF group with respect to the ring plane does not differ significantly from the CH_2 group orientation in cyclopropane. The observed gas-phase molecular structure is related to several theoretical studies of fluorine-substituent effects in cyclopropane derivatives.

Fluorine substitution on a cyclopropane ring is known to have a marked effect on the ring geometry.[1] In 1,1-difluorocyclopropane, a large shortening of the C–C bond between the CF_2 and CH_2 groups is observed, while the C–C bond opposite the CF_2 group lengthens considerably.[2] All the ring bonds shorten in *cis,cis*-1,2,3-trifluorocyclopropane[2] relative to cyclopropane.[4] Hoffmann has discussed the effect of substituents on the cyclopropane ring structure[5] in terms of the Walsh scheme for cyclopropane.[6] However, application of this molecular orbital approach to rings with fluorine substituents does not lead to correct predictions for the ring bond changes.[2,3]

More recently, Deakyne et al. used charge density difference plots obtained from ab initio wave functions to rationalize the experimental ring structure of 1,1-difluorocyclopropane.[7] They identified an additivity rule to correctly predict the ring bond shortening in *cis,cis*-1,2,3-trifluorocyclopropane, to predict the unknown ring geometry of *cis*-1,2-difluorocyclopropane, and to predict the ring structure of 1,1,2,2-tetrafluorocyclopropane,[8] which has been partially determined. In both of these 1,2-fluoro-substituted cyclopropanes, the C–C bond between the methylene and fluoro group is predicted to remain nearly the same as in cyclopropane.[7] This prediction is contrary to the general observation that bonds adjacent to C–F bonds are shorter in the fluorocarbon than in the corresponding hydrocarbon.

An ab initio study by Skancke and Boggs employing complete geometry optimization at the 4-21 level has yielded ring structures for *cis*- and *trans*-1,2-difluorocyclopropane.[9] The calculated differences in the molecular structures of these geometrical isomers are used to explain the absence of the "cis effect" observed for the 1,2-difluorocyclopropanes. In this case, the trans form of 1,2-difluorocyclopropane is 2.8 ± 0.2 kcal/mol lower in energy than the cis form.[10] This result is notable because the cis form

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