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Mechanism of Aromatic Hydrocarbon Acylation by Substituted Benzoic Acids: A Novel Reaction Pathway[1]

P. E. Allegretti, R. D. Bravo, and J. J. P. Furlong

Laboratorio LADECOR, División Química Orgánica, Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, Calles 47 y 115, 1900 La Plata, Argentina

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Abstract—Aromatic hydrocarbons are susceptible to direct acylation by benzoic acids with high yields bearing *ortho* or *para* alkyl groups as substituents under Friedel–Crafts reaction conditions. The α-H of the alkyl moiety seems to be responsible for the observed relatively high reaction rates of conversion. Carbanion-like species are proposed as reaction intermediates, which also operate as strong bases in the reaction rate-determining steps. Trapping experiments, deuterium isotopic effects, and kinetics data favor a concerted reaction pathway where proton transfer from the hydrocarbon molecule to a carbanionic intermediate takes place with a simultaneous electrophilic attack of the carbonylic carbon atom.

INTRODUCTION

The direct acylation of aromatic hydrocarbons by benzoic acids under Friedel–Crafts conditions has been the subject of investigation in regard to its synthetic importance [1–6] and, more recently, to its reaction mechanism [7] (Scheme 1).

In some cases the direct acylation reaction is possible with very good yields, thus omitting the intermediate step of preparation and isolation of the acyl halide, behavior first noticed by Groggins *et al.* [8, 9]. Reiding and Nauta [10] observed a remarkable effect of the *ortho* substituent in the acid molecule when studying the preparation of several benzophenones.

In a previous work [7], it was clearly established that:

(i) Direct acylation is relevant when *ortho* or *para* substitutions with α-H alkyl groups in benzoic acids are present.

(ii) Aluminum chloride is not only a catalyst but also a reagent. Its reaction order is one for 2-alkylbenzoic acids and two for 4-alkylbenzoic acids. These experimental results suggest that $AlCl_3$ is present mainly in its monomeric form.

(iii) The reaction is of first order with respect to benzene for 2-alkylbenzoic acids and of higher than second order for 4-alkylbenzoic acids.

(iv) Initial and fast HCl evolution (equimolar ratio with respect to 2-methylbenzoic acid) is followed by a slow and subsequent HCl evolution during the reaction (equimolar ratio with respect to the 2-methylbenzophenone formed). The total amount of HCl (gas) was determined by titration according to the previously reported methodology [7]. HCl concentration under the experimental conditions is negligible during the reaction.

Additional experimental work has been carried out in order to better define the mechanistic pathway. This task has included the analysis of kinetical runs done with other catalysts, trapping reagents, and labeled compounds.

RESULTS

Preliminary experiments [7, 10] show that the reaction between 2-methylbenzoic acid (**Ia**) and benzene in the temperature range 303–353 K can be selected as the model reaction system for this study. Considering its abnormal relatively high reaction rate, it can be concluded that the *ortho* substitution in the aromatic ring of the benzoic acids plays a relevant role. First order behavior with respect to each reactant is observed until at least 50% conversion (Fig. 1). In the case of the 4-methylbenzoic acid (**Ib**) the reaction shows a higher order with respect to benzene, which actually constitutes an exception to the general kinetic behavior observed. Higher relative rates of conversion to the corresponding benzophenones are also observed for some *para*-substituted benzoic acids.

[1] This article was submitted by the authors in English.

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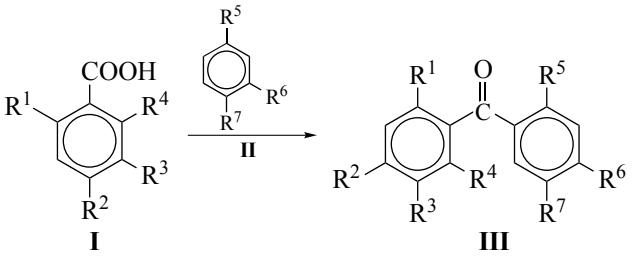


Ia: $R^1 = CH_3$, $R^2 = R^3 = R^4$

Ib: $R^1 = H$, $R^2 = CH_3$, $R^3 = R^4 = H$

Ic: $R^1 = C_2H_5$, $R^2 = R^3 = R^4 = H$

Id: $R^1 = iso\text{-}C_3H_7$, $R^2 = R^3 = R^4 = H$

Ie: $R^1 = R^2 = CH_3$, $R^3 = R^4 = H$

If: $R^1 = R^2 = CH_3$, $R^3 = H$, $R^4 = CH_3$

Ig: $R^1 = CH_3$, $R^2 = H$, $R^3 = NO_2$, $R^4 = H$

Ih: $R^1 = CH_3$, $R^2 = NO_2$, $R^3 = R^4 = H$

Ii: $R^1 = R^2 = R^3 = R^4 = H$

Ij: $R^1 = OH$, $R^2 = CH_3$, $R^3 = R^4 = H$

Ik: $R^1 = Cl$, $R^2 = R^3 = R^4 = H$

Il: $R^1 = OCH_3$, $R^2 = R^3 = R^4 = H$

IIa: $R^5 = R^6 = R^7 = H$

IIb: $R^5 = R^7 = CH_3$, $R^6 = H$

IIc: $R^5 = R^6 = CH_3$, $R^7 = H$

Scheme 1. Benzoic acids (**I**) and hydrocarbons (**II**) employed in this study.

The temperature effect on the reactions investigated is reflected in the activation parameters for the different substituted benzoic acids (Table 1). There are six cases (**Ia**, **Ig–Ii**, **Ik**, **Il**) where the observed reaction rates are at least one order of magnitude slower than that found for the acylation with **Ia** (the model reaction system) under the same experimental conditions.

A primary isotope effect (k_H/k_D = 3.5) [7] can be observed for the reaction of 2-methylbenzoic acid-d_4-methyl-d_3 ($CD_3C_6D_4COOH$), which supports a C–D molecular bond rupture involved in a reaction rate-determining step. In fact, the corresponding mass spectrum of the acylation product shows deuterium–hydrogen exchange in the methyl group of the substituted benzoic acid suggesting a carbanionic-like structure in the corresponding reaction pathway (Fig. 2b). Instead, no isotopic exchange could be detected, as expected, in the aromatic ring of the substrate molecule. No isotopic exchange was observed in the methyl group of the deuterated acid using the same reaction setup but with cyclohexane as a solvent.

Trapping experiments were carried out by using cyclohexanone as an electrophile to find carbanionic-like intermediate participation. One of the reaction products, 2-(2-hydroxy-2,2-pentamethylenethyl)benzoic acid (c.a. 5% yield), was detected by GC–MS analysis. It might come from the hydrolysis of the expected lactone (Eq. (I)). The corresponding mass-spectrometric data (*m*/*z* 43 (42.8%); 56 (25.7); 57 (100); 70 (17.1); 71 (85.7); 85 (31.4); 91 (14.3); 95 (5.7); 96 (11.4); 99 (8.6); 104 (9.0); 113 (8.1); 118 (11.4); 135 (2.9); 136 (10.2); 163 (6.0); 178 (3.4); 188 (2.3); 189 (2.0); 206 (3.2); 216 (4.0); 217 (2.6)) indicate that the molecular ion (*m*/*z* 234) is absent, which is supported by logical neutral losses in the high mass region of the spectrum:

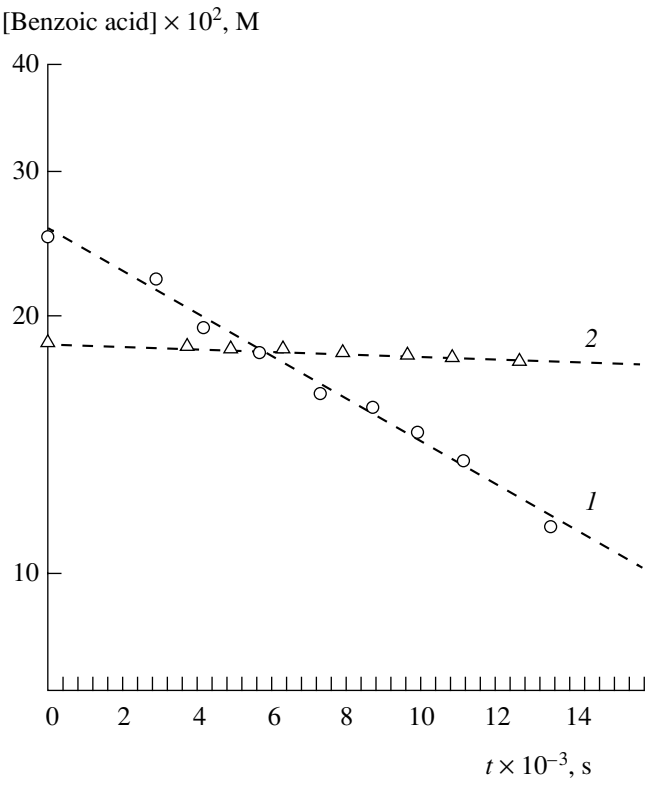


Fig. 1. Typical semilogarithmic plots for the rate constant determinations of the acylation reaction with $AlCl_3$ at 353 K: (*1*) benzene with 2-methylbenzoic acid; (*2*) benzene-d_6 with 2-methylbenzoic acid.

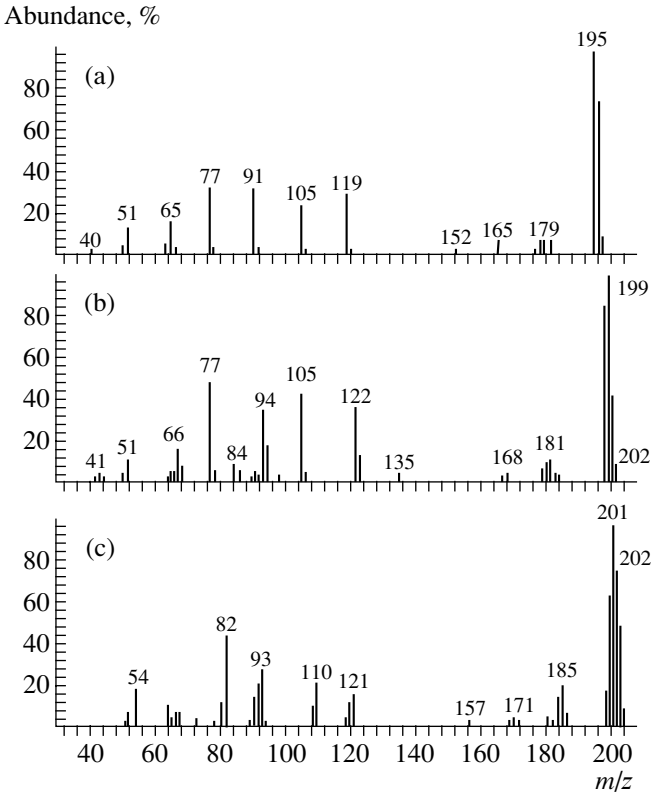
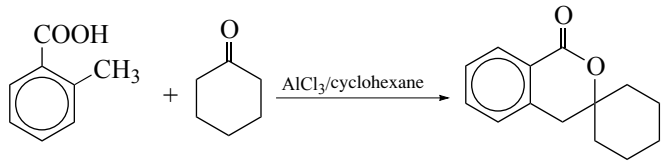


Fig. 2. Mass spectra of 2-methylbenzophenone (a) completely hydrogenated; (b) partially deuterated as comes from the reaction of benzene with 2-methylbenzoic acid-d_4-methyl-d_3; (c) partially deuterated from the reaction of benzene-d_6 with 2-methylbenzoic acid.

the fragment peaks $(M–OH)^+$, $(M–H_2O)^+$, $(M–COOH)^+$, and $(M–HCOOH)^+$ are in fact observed. That fragmentation pattern (Scheme 2) supports the postulated structure of the reaction product shown in Eq. (I).



(I)

In the acylation reactions of benzene-d_6 with 2-methylbenzoic acid (**Ia**) and 2,4-dimethylbenzoic acid (**Ie**), the values of the primary isotopic effects observed (k_H/k_D = 5.5 and 9.2, respectively) demonstrate that the C–D molecular bond rupture in the hydrocarbon molecule is involved in the rate-determining step of the reaction. Furthermore, the mass spectra obtained for both 2-methylbenzophenones, hydrogenated and partially deuterated (Figs. 2a and 2c), show that partial deuteration certainly takes place, one of the main species being the 2-methylbenzophenone-d_5-methyl-d_2 (*m*/*z* 203). Analogous conclusions can be drawn examining the mass spectrum of the partially deuterated 2,4-dimethylbenzophenone product (Fig. 3, *m*/*z* 217).

The determinations of the reaction orders for benzene (using cyclohexane as a cosolvent) and for $AlCl_3$ were also carried out for the acylation with 2-hydroxy-4-methylbenzoic acid (**Ij**). These results are similar to the corresponding values obtained for the acylation with 4-methylbenzoic acid (**Ib**) [7] (Tables 2 and 3).

DISCUSSION

From previous results [7], we can conclude that the *ortho* and *para* alkyl substitution (with free α-H) in the benzoic acid molecule is responsible for higher relative rates of conversion to the corresponding benzophenone products; the aluminum halide employed is not only a catalyst but also a true reactant in the reactions investi-

Table 1. Rate constants and activation parameters for the acylation reactions of substituted benzoic acids in a benzene solution in the presence of $AlCl_3$

Benzoic acid	$k \times 10^8$, $M^{-1}\ s^{-1}$			$\Delta H^{\neq}$, kJ/mol	$\Delta S^{\neq}$, J $mol^{-1}\ K^{-1}$
	353 K	323 K	303 K		
Ia	555 ± 27	47.6 ± 2.5	14.0 ± 0.3	61.8 ± 3	–172 ± 17
Ia[1]	626 ± 30	654 ± 2.5	16.2 ± 0.7	61.8 ± 2	–171 ± 16
Ia[2]	562 ± 20	73.2 ± 3.5	15.8 ± 0.1	61.8 ± 1	–175 ± 3
Ia[3]	572 ± 30	76.1 ± 3.0	15.2 ± 3	59.9 ± 3	–177 ± 17
Ia[4]	4.14 ± 0.2	0.79 ± 0.03	0.21 ± 0.01	49.8 ± 1	–247 ± 7
Ib	187 ± 7	34.9 ± 1.5	9.5 ± 0.3	49.9 ± 2	–215 ± 6
Ib[1]	170 ± 8	36.6 ± 1.5	11 ± 0.5	45.5 ± 1	–228 ± 5
Ib[2]	102 ± 8	23.8 ± 1.5	5.93 ± 0.25	48.7 ± 3	–222 ± 9
Ic	1100 ± 50	117 ± 5	20 ± 1	67.6 ± 2	–150 ± 8
Id	1950 ± 40	266 ± 2	48.6 ± 0.6	62.6 ± 3	–159 ± 7
Ie	579 ± 26	474 ± 2	9.5 ± 0.4	70.2 ± 3	–148 ± 9
If	151 ± 2	38.6 ± 0.9	9.0 ± 0.5	46.9 ± 3	–225 ± 8
Ig	20.6 ± 0.9	5.5 ± 0.2	2.0 ± 0.1	38.6 ± 2	–265 ± 7
Ih	6.49 ± 0.07	1.94 ± 0.06	0.78 ± 0.04	34.8 ± 2	–285 ± 5
Ii	60.4 ± 0.8	7.0 ± 0.2	1.2 ± 0.3	64.9 ± 2	–181 ± 15
Ij	108.6 ± 5.4	16.1 ± 0.7	5.27 ± 0.35	56.5 ± 3.4	–192 ± 18
Ik	33.0 ± 1.5	–	–	–	–
Il	9.3 ± 0.5	–	–	–	–

[1] In *p*-xylene solution.
[2] In *m*-xylene solution.
[3] In benzene solution and $AlBr_3$ as catalyst.
[4] In benzene solution and F_3CSO_3H as catalyst.

gated, and that the C–H bond rupture in the α-C of the alkyl group seems to be involved in the rate-determining step of the reaction. The relative acidity of the molecular alkyl α-H is a relevant factor in the reaction rates observed, a fact which is supported by the kinetic results if the proposed reaction pathway involves the hydrocarbon interaction with carbanionic-like species (Scheme 3, Table 1). Thus, the introduction of a withdrawing substituent in C-5 of the benzoic acid molecule increases the relative acidity of the α-H in C-2 (acylation reaction with **Ig**). The nitro group as a substituent also increases the electrophilicity of this acid, as it does in **Ih** when the nitro group is in C-4. Instead, an extra methyl group in C-4 in the case of the reaction with **Ie** exerts the opposite effect, decreasing both the acidity of the 2-methyl groups and the electrophilic character of the molecule.

Taking into account that the first step in Scheme 3 can be kinetically disregarded (and irreversible), that HCl does not accumulate in the reaction medium (present in a very low saturation concentration), and that $[AlCl_3]$ is nearly constant during the reaction (the AlClO accounts for the $AlCl_3$ initially involved in the fast acid–base step), the corresponding kinetic equation would be as follows:

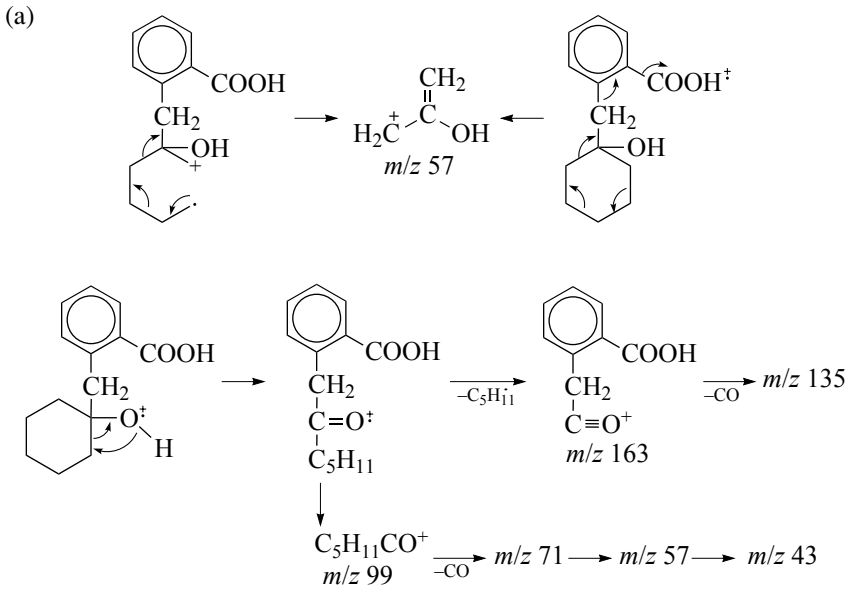
$$r = k[\text{Benzoic acid}][\text{ArH}],$$

$$k = k_C[AlCl_3],$$

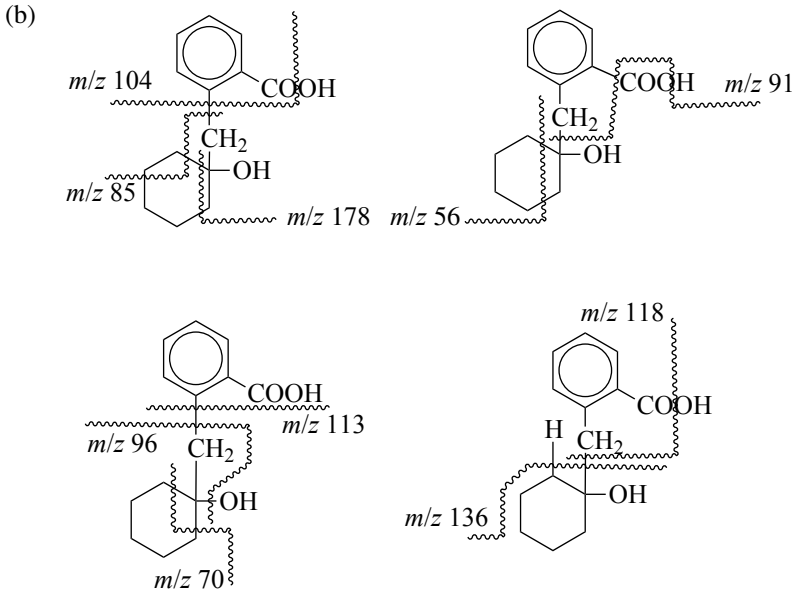
where k_C takes care not only of the carbanionic-like intermediate concentration in the reaction mixture but also of the catalytic action of the Lewis base. In the case of 4-methylbenzoic acid (**Ib**), k_C also takes care of the concentration of the intermediate coordinated with an extra $AlCl_3$ molecule (Fig. 4).

The fact of considering [$AlCl_3$] as "nearly constant" is based on the assumption that it exists mainly in a single form; otherwise, the kinetics would not behave as observed. The calculation of free [$AlCl_3$] is not a simple procedure, but its constant concentration may be explained taking into account that coordination is relatively minor in all the carbonyl-containing species or assuming that the free halide concentration in the corresponding equilibria does not depend on the nature of the carbonyl compound (very similar equilibrium constant values); otherwise, the free halide concentration would change with the progress of the reaction, which is not observed.

The relatively low second-order reaction rate for 4-methylbenzoic acid (**Ib**) in Table 1 can be explained due to the fact that all calculations were done in terms of a second-order reaction rate. Here the transition state of the rate-determining step for the acylation of **Ib** would involve three moieties: the carbanionic-like reaction intermediate (Fig. 4) and two benzene molecules. On the other hand, the relatively smaller enthalpy



Other importants observed are:



Scheme 2. Main fragmentation pathways derived from the mass spectrum of the trapping experiment product.

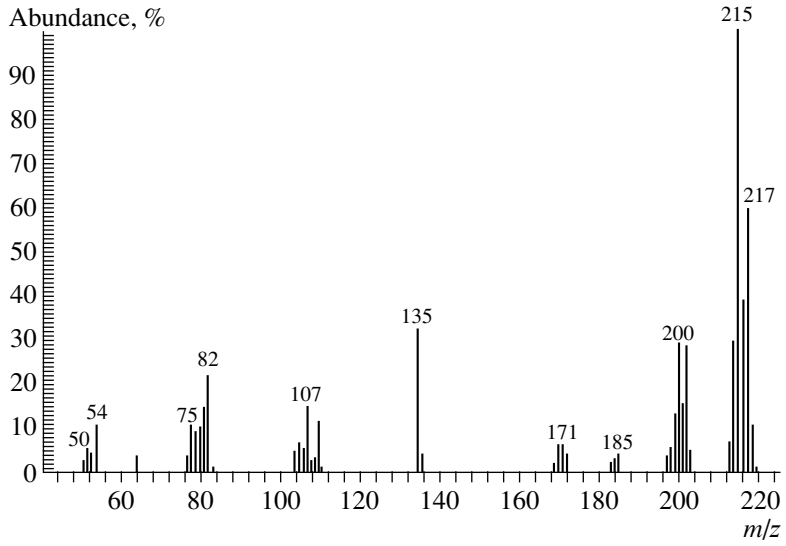


Fig. 3. Mass spectrum of 2,4-dimethylbenzophenone-d_5-methyl-d_x.

of activation change observed as compared with **Ia** could be explained through the corresponding reaction intermediate stability. The charge repulsion for the dianionic intermediate in the acylation with **Ib** should be lower than the analogous one for **Ia**. It is evident that, in the case of the reaction intermediate that corresponds to the acylation with **Ia**, it is not necessary to include an extra $AlCl_3$ molecule, since the same molecule that reacts with the alkyl group can be coordinated to the carbonylic oxygen atom (Scheme 3).

The intermediate structure for the reaction of **Ib** depicted in Fig. 4 not only reflects the second-order rate with respect to the halide but also the multiple-order rate with respect to the hydrocarbon (the hydrogen-donating species in the reaction system).

For the acylation reaction with 2-methyl-4-nitrobenzoic acid (**Ih**), the operating position of the nitro group decreases the activation enthalpy change as compared with the 2-methyl-5-nitrobenzoic acid (**Ig**) (34.8 ± 2 and 38.6 ± 2 kJ/mol, respectively).

Good linear relationships are obtained according to Leffler and Exner criteria for most of the reactions investigated with the exception of the acylation with benzoic acid (**Ii**), as well as the acylation with **Ia** using trifluoromethanesulfonic acid as a catalyst (Fig. 5). For these and the other slow acylation reactions investigated (**Ik** and **Il**), it looks likely that they proceed by a different reaction mechanism.

Table 2. Determination of benzene reaction order for the acylation reaction with 2-hydroxy-4-methylbenzoic acid (**Ij**) at 353 K using cyclohexane as a cosolvent[a]

[Benzene], mol/l	$k \times 10^7$, s^{-1}
3.1	9.4 ± 0.5
5.2	39.8 ± 2.5
10.0	148.0 ± 8.5
$n_1 = 2.4$ (corr. coeff. = 0.990)	

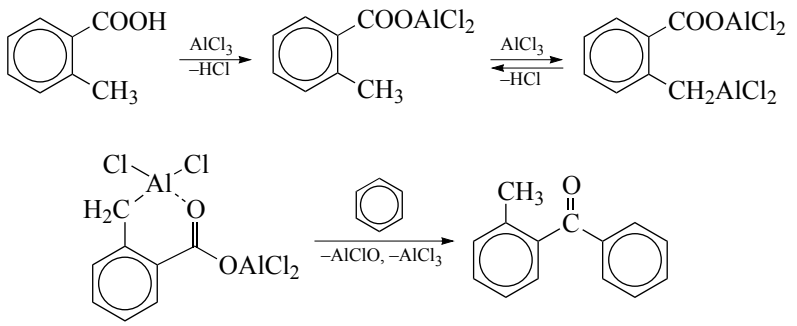
[a] The corresponding rate constant equation is: $k = k_0 \times [\text{benzene}]^{n_1}[AlCl_3]^{n_2}$.

Table 3. Determination of $AlCl_3$ reaction order for the acylation reaction with 2-hydroxy-4-methylbenzoic acid (**Ij**) at 353 K[a]

$[\mathbf{Ij}]_0$, mol/l	$[AlCl_3]_0$, M	$[AlCl_3]^b$, M	$k \times 10^7$, s^{-1}
0.043	0.11	0.067	135 ± 6.2
0.046	0.094	0.048	61.6 ± 2.8
0.048	0.082	0.034	9.3 ± 0.5
$n_2 = 1.94$ (corr. coeff. = 0.998)			

[a] The corresponding rate constant equation is: $k = k_0[\text{benzene}]^{n_1}[AlCl_3]^{n_2}$. $[\mathbf{Ij}]_0$: initial molar concentration of hydroxy-4-methylbenzoic acid; $[AlCl_3]_0$: initial molar concentration of $AlCl_3$.

[b] The concentration of $[AlCl_3]$ is $[AlCl_3]_0$–$[\mathbf{Ij}]_0$ due to the first fast and irreversible reaction step. For this reaction order determination it is assumed that the reagent is the first intermediate in Scheme 3. The actual $[AlCl_3]$ is directly proportional to the absolute amount of the halide in the reaction mixture.



Scheme 3. Reaction pathway for the acylation with 2-methylbenzoic acid.

The results of the kinetic study for the acylation reaction with 2-hydroxy-4-methylbenzoic acid (**Ij**) are consistent with the formation of a carbanionic species as intermediate ($\Delta H^{\#} = 56.5 \pm 3.4$ kJ/mol). Although it is recognized that the acidic character of the hydroxyl group is high enough to easily react with the aluminum halide, the resulting phenolate is not basic enough to efficiently participate in the proton transfer involved in the rate-controlling step. The activation enthalpy change in this case is increased due to the presence of an electron-releasing group (hydroxyl), which decreases both the acidity of the methyl group and the electrophilicity of the carbonylic carbon atom in the molecule. To determine if the same type of mechanism applies with **Ij**, the reaction order calculations performed demonstrate that the aluminum chloride and the benzene reaction orders are nearly two (Tables 2 and 3). The isokinetic relationship in this case also supports that proposal.

The primary isotopic effect observed when carrying out the acylation reaction with 2-methylbenzoic acid-d_4-methyl-d_3 ($k_H/k_D = 3.5$) suggests that the formation of carbanionic-like species is determining the reaction rate, although is not necessarily supposed to be the slow step in the actual reaction mechanism. The existence of a preequilibrium involving dianion formation as an intermediate can be postulated by considering the observation of 2-methylbenzophenone completely hydrogenated as a reaction product (Fig. 2b). The relative amount of both partially and totally hydrogenated methylbenzophenones is the result not only of the value of the CH/CD bond strengths ratio but also of the proton availability in the reaction medium.

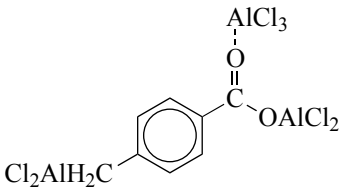


Fig. 4. Carbanionic intermediate for the benzene acylation reaction with 4-methylbenzoic acid (**Ib**).

In relation to the primary isotope effects observed for the acylation reaction of benzene-d_6, it can be proposed that the rupture of the C–D bond in the hydrocarbon is involved in one of the determining steps of the reaction. The existence of completely deuterated species in the corresponding mass spectrum (Fig. 2c) indicates the occurrence of a fast exchange process previous to the final attack of the hydrocarbon molecule. The fact that most of the benzophenone observed is partially hydrogenated suggests the existence of a preequilibrium and that the hydrogen chloride could be the main proton-donating agent in the exchange reaction. Further H/D exchange due to the benzophenone formation reaction equilibrium is disregarded, since this is certainly a nonreversible process. Thus, the general reaction pathway already proposed for the acylation with 2-methylbenzoic acid (Scheme 3) finds additional support.

Other Alternative Mechanistic Proposals

Other alternatives to the proposed mechanism have also been considered as it is the case of the preliminary formation of the corresponding acyl halide that has been claimed to be operative in the mechanism of the direct acylation reaction [11], although this type of intermediate has not been so far detected. Besides, the rate of formation of the alkyl benzophenones from the corresponding benzoic acids is one order of magnitude smaller than the figures worked out from the corresponding acyl halides (in the case of 2-methylbenzoyl chloride, $k = 4.19 \times 10^{-5}$ M^{-1} s^{-1} at 353 K). Not only does it seem that detection of the halide should be possible, but also, if its formation is considered to be the rate-controlling step (reaction between the acid and the $AlCl_3$), most of the kinetic data here reported do not have any reasonable explanation.

In the case of the reaction pathway proposed in Scheme 4a (although the occurrence of the paired $C_6H_5^-$ can be considered somehow unrealistic), the effect of the nature of the hydrocarbon should be noticeable. Besides, this reaction pathway does not justify the high hydrocarbon reaction order obtained for the 4-alkylbenzoic acids. In an alternative reaction

pathway (Scheme 4b), the presence of an alkyl group in *ortho* or *para* position does not seem to be consistent with the reaction rate increase actually observed. Besides, it does not account for the observation of di- and trideuterated species when benzene-d_6 was employed as a reactant. Furthermore, the other mechanistic proposal (Scheme 4c) does not justify the higher reaction order observed for the hydrocarbon in the case of the acylation with 4-alkylbenzoic acids and the lack of the hydrocarbon nature effect, as mentioned above, for the mechanism displayed in Scheme 4a. On the other hand, the highly unstable ketene structure postulated makes less likely this reaction pathway in comparison with that one where the intermediate keeps being aromatic. Alternatively, the adduct formation shown in Scheme 4d cannot be the reaction-controlling step, since not only the methyl-d_2 species would not be noticeable for the reaction with benzene-d_6 but the primary isotopic effect would not be observable either. Notwithstanding this, if the slow step of the reaction were the last one shown in either Schemes 4b or 4d, a noticeable hydrocarbon effect would be observed.

The apparent lack of sensitivity to the substitution in the hydrocarbon molecule may allow us to propose an alternative concerted mechanism where the acyl attack to the hydrocarbon and proton transfer to the carbanion occurs synchronously (Fig. 6). The concerted mechanism gets rid of the objection for the phenyl anion occurrence (Schemes 4a and 4c). In the case of 4-alkylbenzoic acid reactions, the concertness can be explained through the participation of more than one hydrocarbon molecule (the reaction solvent) in the corresponding transition state. This proposal is also consistent with the primary isotopic effects actually observed for the 2-methyl and 2,4-dimethylbenzoic acids (k_H/k_D = 5.5 and 9.2, respectively). For the latter acid molecule, the proton-transfer process seems to be relatively more relevant than the electrophilic attack in the transition state due to the substituent effect on the carbonylic carbon electron density.

EXPERIMENTAL

Materials

The benzoic acids employed in this study were synthesized and purified according to procedures previously reported [7].

Benzene (Merck p.a.) was heated under reflux over sodium and distilled before use.

Anhydrous aluminum chloride (Carlo Erba RRE, 98%), benzene-d_6 and 2-methyl-benzoic acid-d_4-methyl-d_3 (Aldrich, 99.9% minimum isotopic purity) were used without further purification.

Cyclohexane (Kodak, yellow label) was distilled with molecular sieve 4 Å.

Cyclohexanone (Kodak, white label) was distilled at 20 Torr (bp 50°C).

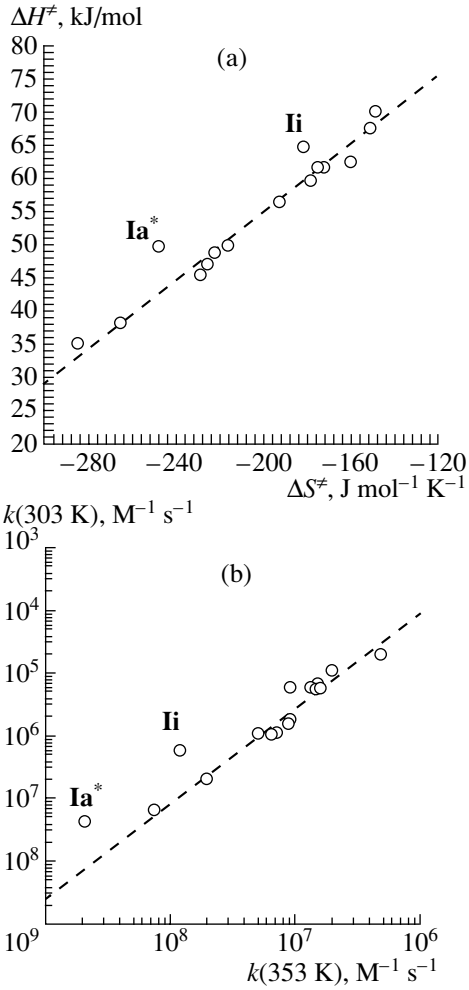


Fig. 5. (a) Isokinetic relationship and (b) Exner relationship plots for acylation reactions of an aromatic hydrocarbon by benzoic acids. * In benzene solution and F_3CSO_3H as catalyst.

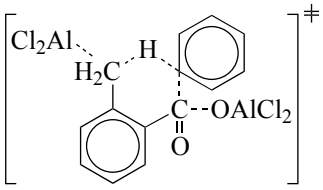


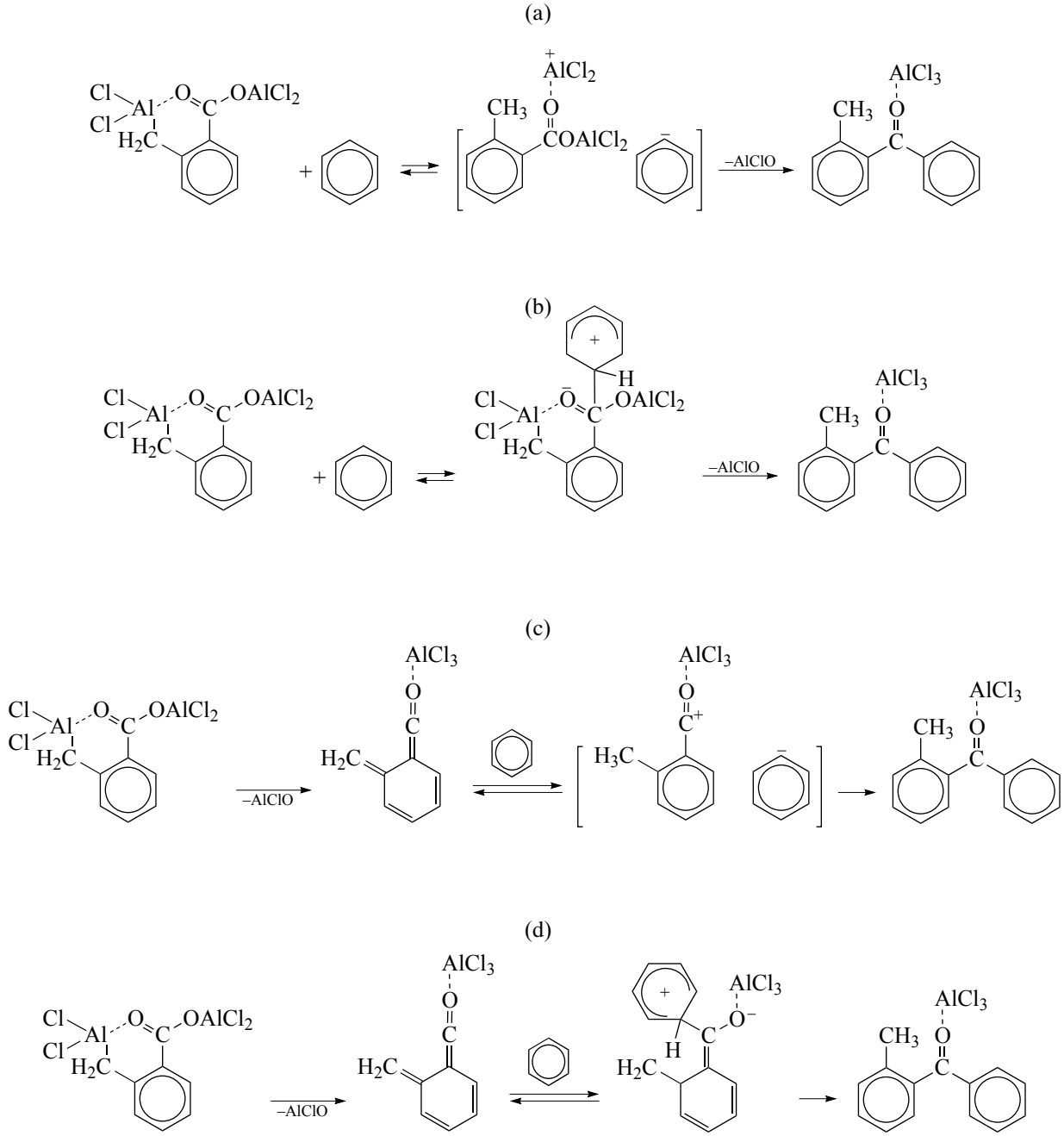
Fig. 6. Postulated transition state structure for the rate-controlling step of the benzene acylation reaction with 2-methylbenzoic acid.

Kinetic Methods

Kinetic runs were performed in a four-necked Pyrex round flask to allow vigorous mechanical stirring, precise temperature monitoring (±0.1°C), suitable connection to a condenser, passage of a nitrogen stream, and convenient sampling. All the kinetic experiments, including those for evaluating isotopic effects, were performed at least twice using a 2.2 : 1 $AlCl_3$: substi-

tuted benzoic acid molar ratio. In a typical experiment, 24 mmol of the corresponding benzoic acid was dissolved in 80 ml of the aromatic hydrocarbon, and then 52.8 mmol of $AlCl_3$ was quickly incorporated with vigorous stirring. It should be noted that this halide is not very soluble in the solvents used and that a phase equilibrium takes place, so that the actual [$AlCl_3$] after the first fast acid–base reaction is small and directly proportional to the amount of the halide in the reaction mixture.

After selected times, 5-ml aliquot portions were periodically withdrawn and the reactions were quenched by mixing with 10 ml of a 20% aqueous NaOH solution. After vigorous shaking, aliquots of the organic layer were weighed out and conveniently diluted with toluene determining the corresponding dilution factor. In all the cases, the reaction mixtures remained colorless after this treatment. Under these conditions no products other than benzophenones were observed. The kinetic determinations showed typical



Scheme 4. Alternative proposals for the reaction mechanism.

pseudo-first-order rate behavior for the different benzoic acids (Fig. 1). The concentrations of the benzophenones in the organic layer were monitored spectrophotometrically [7].

Isotopic Effect Determinations

The synthesis of deuterated 2-methylbenzophenones and their reaction rate measurements in a benzene-d_6 solution were carried out with 2-methylbenzoic acid (Fig. 1) and 2,4-dimethylbenzoic acid (**Ia** and **Ie**, 3.7 mmol) in the presence of $AlCl_3$ in the usual molar ratio. For the preparation, after 4 h of refluxing, the reacting mixture was dropped into a cold aqueous hydrochloric acid solution (0°C) followed by extraction with toluene (3 × 7 ml). Then, the organic layer was washed twice with 10% aqueous $NaHCO_3$ (10 ml) and finally with distilled water. The organic extract was dried over anhydrous Na_2SO_4 and filtered off; the solvent was removed under reduced pressure. After molecular distillation of the residue (0.1 Torr, 80°C), a clear yellowish oil was finally obtained (25 and 11% yields, respectively, which are consistent with the relative values of the corresponding rate constants).

Trapping of the Carbanionic Reaction Intermediate

2-Methylbenzoic acid (8.3 mmol), $AlCl_3$ (18.3 mmol), and cyclohexanone (12 mmol) used as the electrophilic reagent were incorporated into cyclohexane (40 ml). After 1 h of mechanical stirring at room temperature and an additional 2 h at 80°C, the reaction system was dropped into a cold hydrochloric acid solution. The corresponding toluene extract was dried with anhydrous Na_2SO_4, and the solvent was evaporated at a reduced pressure. The reaction products were analyzed by GC–MS.

Spectrometric Measurements

The UV determinations were performed with a model HP 8452A Hewlett-Packard diode array spectrophotometer. The GC–MS experiments were run in a model HP 5890 II Plus chromatograph coupled with a HP 5972A mass-selective detector.

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