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STUDIES IN TRIFLUOROMETHANESULPHONIC ACID—IV

KINETICS AND MECHANISM OF ACYLATION OF AROMATIC COMPOUNDS

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Abstract—A detailed kinetic study has been made of acylation reactions in solvent trifluoromethanesulphonic acid (CF_3SO_3H) using carboxylic acids as the precursors to the electrophilic species involved. These species were shown to be probably the protonated form of the mixed anhydride. The reactions show high substrate selectivity characterised by high negative values of ρ^+. Substituents in the carboxylic acids have a relatively small influence on the reactions rates due to a cancellation of substituents effects on the protonation of the mixed anhydride with those operating on the subsequent slow reaction of these species with the aromatic substrate. Anomalous effects were found for certain ortho substituents. The overall mechanism is discussed in terms of polar and steric effects in conjunction with the competing protonation of the aromatic bases, together with evidence from isotope effects.

Acylation is an extremely well known and synthetically useful reaction, and has been the subject of extensive reviews.[2-6] The mechanism of the Lewis acid catalysed processes has been investigated by a number of workers. The reaction is generally characterised by high substrate selectivity (k toluene/k benzene > 100) and high positional selectivity.[7] Brown *et al.*[7,8] have studied the kinetics of acetylation using $CH_3COCl/AlCl_3$ in 1,2-dichloroethane for an extended range of methylated benzenes and concluded that large steric requirements are apparent for the reaction. The reaction was found to be first order in hydrocarbon and in acetyl chloride–aluminium chloride complex. The nature of the electrophilic species was considered to be not the free acylium ion, but a donor–acceptor complex formed by coordination of the $AlCl_3$ via the oxygen atom of the acyl moiety.

Olah[9,10] has conducted a study covering a much wider range of Lewis acids in solvents nitromethane and nitrobenzene, and has found very similar effects to those obtained in non polar solvents. However, relatively large kinetic isotope effects were found, which suggested that the conversion of σ intermediates to products is at least partially rate determining.

Benzoylation in nitrobenzene shows complex kinetics with third order rate constants decreasing with increasing Lewis acid concentration.[11,12] Mixed anhydrides of the type $R.CO.O.SO_2CF_3$ have been shown to be excellent reagents for the synthesis of acyl derivatives.[13] Accordingly, trifluoromethanesulphonic (triflic) acid CF_3SO_3H itself should act as an efficient catalyst in acylation. The present work, which is a continuation of a detailed kinetic study of reactions in this versatile solvent, reports on acylation of various aromatic substrates using carboxylicaacids as precursors to the acylating agents.

RESULTS AND DISCUSSION

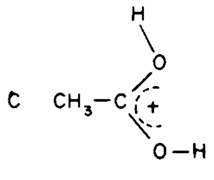
The acylations were carried out using a range of carboxylic acids as precursors, and following the rates of reactions by NMR spectroscopy. Triflic acid is a very strong protic acid, and as such should be capable of protonating carboxylic acids and generating the corresponding acylium ion according to eqn (1):

$$RCO_2H + HX \overset{K_A}{\rightleftarrows} RCO_2\overset{+}{H}_2 + \bar{X} \overset{K_{A'}}{\rightleftarrows} R\overset{+}{C}O + H_2O + \bar{X}. \tag{1}$$

Attempts have been made to distinguish between the protonated carboxylic acid and the acyl cation from NMR chemical shifts and IR data. In a study of $CH_3COCl:MX_n$ complexes (M = Sb,As; X = F, Cl), Olah[14] found very strong bands in the IR at ~2300 cm^{-1} which were assigned to $CH_3\overset{+}{C}O$. The ^1H NMR spectra, however, showed two sharp singlets at 4.68 and 2.94 ppm. The former was assigned to the free cation whereas the latter was considered to be due to the complex $CH_3C(F)=O \rightarrow MX_n$(I). The spectrum of C_6H_5COF in SbF_5/SO_2 solution appeared to be wholly due to the free cation. Deno and Charles[15] examined the protonation of a series of carboxylic acids in aqueous H_2SO_4 and H_2SO_4/SO_3 media by NMR spectroscopy. They concluded that for acetic acid, the free cation only occurred in the most highly acidic media (2:3 H_2SO_4/SO_3) and that in the concentrated (98%) acid itself, the predominant species was the protonated acid.

Hogeveen[16] has reported the existence of two isomeric forms 2 and 3 of protonated acetic acid in $HF-BF_3$ solution at −80° with $\delta_{Me} = 2.87$ ppm. This was confirmed by Olah and White[17] using $FSO_3H/SbF_5/SO_2$ solution at −60° ($\delta_{Me} = 3.18$), and they were able to show that between −30° and 0° conversion to the acyl cation occurred ($\delta_{Me} = 4.35$ ppm) at a measurable rate.

Schubert *et al.*[18] have also reported acylium ion formation from mesitoic acid in H_2SO_4/SO_3 mixtures and showed that $R\overset{+}{C}O$ was formed in about 50% yield in 98% H_2SO_4 at 35° (*cf* cryoscopic data below). Fluorosulphuric acid is even more effective at producing the mesitoyl cation (100% at 25°).[19]



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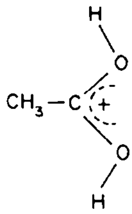

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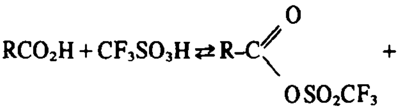
trans

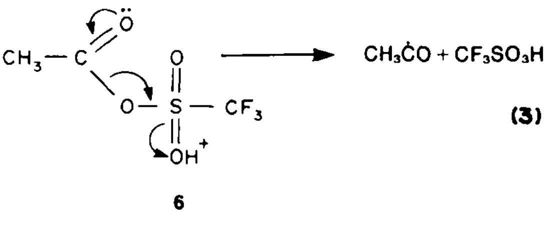
The results of these studies and data for triflic acid appear in Table 1. The chemical shifts for CF_3SO_3H listed in the Table agree well with those previously assigned to the protonated acid. Another possible structure for the acylating agent, however, is the mixed anhydride,



$$RCO_2H + CF_3SO_3H \rightleftarrows R{-}C\begin{matrix} {\diagup}O \\ {\diagdown}OSO_2CF_3 \end{matrix} + H_2O. \quad (2)$$

These species have already been shown to be extremely powerful acylating agents.[13] It is interesting to note in this context that in concentrated H_2SO_4, the mesitoyl cation is apparently fully formed as determined by cryoscopic measurements.[20] Since triflic acid is a stronger acid than sulphuric acid, the mesitoyl cation should also be formed quantitatively in the former. NMR evidence suggests that it is not, which offers indirect support for the mixed anhydride $R\overset{O}{C}{-}OSO_2CF_3$ as the acylating agent.

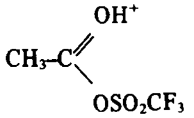
A detailed spectroscopic study of acetic anhydride in triflic acid has led to the identification of several protonated species.[21] At mole ratios of $(CH_3CO)_2O:CF_3SO_3H$ of less than 0.2, the acylium ion **4** and the diacetyl acetylium ion **5**[22] were characterised. These ions were formed from the mixed anhydride, as deduced from the disappearance of IR bands at 1815 and 1310 cm^{-1} assigned to the latter and the increase in intensity of bands at 2300 and 2200 cm^{-1} assigned to the species **4** and **5** respectively. The formation of the acylium ion is favoured by sulphonyl oxygen protonation **6** and hindered by carbonyl protonation of the mixed anhydride.



(3)

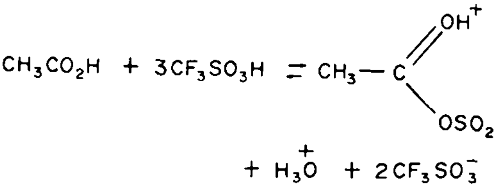
6

In contrast, it was not possible to detect the acylium ion even using low temperature NMR (−40°) in solutions of acetic acid in CF_3SO_3H. The chemical shift of the methyl protons was 2.93 ppm, which is in excellent agreement with our own value and close to that observed for the $CH_3CO_2H_2^+$ ion. If the mixed anhydride were formed to any significant extent, then presumably it will be carbonyl protonated since no acylium ion is produced in this system.



7

The methyl group should therefore be more deshielded than that of the acidium ion due to electron withdrawal by the triflate group. Cogent arguments against significant mixed anhydride formation come from an examination of the detailed conductivity measurements of Russell and Senior[23] for water and acetic acid in CF_3SO_3H. The overall process for the formation of the mixed anhydride is as follows:



$$CH_3CO_2H + 3CF_3SO_3H \rightleftarrows CH_3{-}C\begin{matrix} {\diagup}OH^+ \\ {\diagdown}OSO_2CF_3 \end{matrix} + H_3\overset{+}{O} + 2CF_3SO_3^- \quad (4)$$

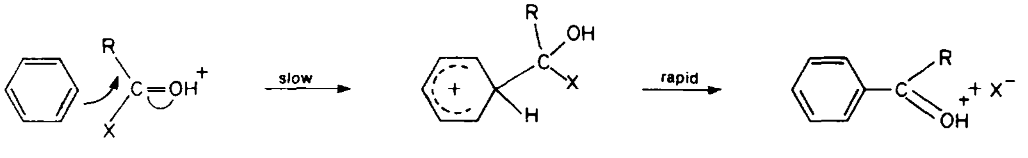
If this reaction occurs to any great extent, then the conductivity of solutions of acetic acid should be much greater than those of water in CF_3SO_3H. This is not the case. The specific conductivity-concentration curves for CH_3CO_2H and H_2O coincide almost exactly over the concentration range 0–0.18 M, showing that the acidium ion is the principal species present in solution.

$$\begin{gathered} RCO_2H + HX \rightleftarrows RCO_2\overset{+}{H_2} + \bar{X} \\ [X = CF_3SO_3]. \end{gathered} \quad (5)$$

Evidence will be presented later which confirms that electrophilic attack is not by the acylium ion. However, one cannot completely rule out reaction via species **7** which could be present in concentrations too small to be detected by IR and NMR spectroscopy.

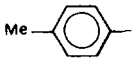
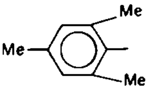
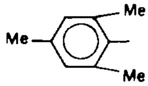
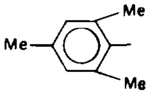
Evidence for **7** as an intermediate comes from rate studies. The basicities of the acids used in this study lie in the pK_{BH^+} range of −6 to −8[24] and in a medium of such high acidity ($H_0 = -14.6$ see Ref. 25) all should be completely protonated, and thus factors governing the protonation of the carboxylic acid become irrelevant. The reaction rate is then dependent on steric and polar effects on the reaction of this ion with the aromatic substrate. On this basis acetic acid should react slower than formic acid due to increased steric effects. However the reverse is true, acetic acid being some 50 times faster. It therefore seems likely that the protonated mixed anhydride is the true acylating agent leading to the following mechanism (eqn 6) (*cf* Ref. 21).

The product ratios for the reaction of toluene with formic acid and acetic acid in CF_3SO_3H, appear in Table 2. The results are consistent with reaction via **7** on two grounds. Firstly, the reaction is highly selective, and the selectivity is increased when a more bulky carboxylic acid is used. In this context, it is worth recalling the lack of selectivity found in the 2, 4, 6-tribromobenzoylation of aromatic compounds[26] which is consistent with a free acyl cation attack. Secondly, if such free ions were fully



(6)

Table 1. Chemical shifts (δ ppm relative to TMS) of methyl groups of protonated acids (A) and acyl cations (B) derived from carboxylic acids RCO_2H in acidic media

R	Solvent system	δ_A	δ_B	Ref.
CH_3	$SbCl_5$	2.94	4.68	14
CH_3	FSO_3H–SbF_5–SO_2	3.18	4.35	17
CH_3	H_2SO_4/SO_3	2.67	3.93	15
CH_3	HF/BF_3	2.87	3.93	16
CH_3	CF_3SO_3H	2.90	—	This work
	CF_3SO_3H	2.90	—	This work
	CF_3SO_4/SO_3	2.43[a] 2.34[b]	2.73[a] 2.60[b]	15
	FSO_3H	— —	2.75[a] 2.62[b]	19
	CF_3SO_3H	2.50[a] 2.35[b]	— —	This work

[a,b]Values for ortho and para-methyl substituents respectively.

Table 2. Product yields and ratios for the reaction of formic acid and acetic acid with toluene in CF_3SO_3H at 25°. 0.5 M in each reagent

RCO_2H	Time (h.)	% Reaction	Product ratios %		
			o	m	p
HCO_2H	1	1.8	6.0	—[a]	94
HCO_2H	2	3.0	6.1	—	93.9
HCO_2H	5	7.4	6.4	—	93.6
CH_3CO_2H	0.25	66	—	—	≈98
CH_3CO_2H	1	76	0.97	0.78	98.3
CH_3CO_2H	2	99	0.97	0.75	98.3

[a]No meta detected.

Table 3. Second order rate constants (k_2^{obs}, l mol^{-1}, s^{-1}) for acylations using carboxylic acids in CF_3SO_3H at 25°

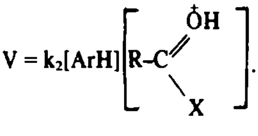
Substrates[a]	Acids[a]	$10^5 k_2^{obs}$
Benzene	p-toluic acid	1.1
Toluene	p-toluic acid	166
Toluene	HCO_2H	9.5
Toluene	CH_3CO_2H	480
Toluene	CF_3CO_2H	no reaction
Toluene	mesitoic acid	3.5
Mesitylene	p-toluic acid	2440
Mesitylene	mesitoic acid	no reaction

[a]Concentrations equimolar at 0.2 M.

formed, then $H\overset{+}{C}O$ should react faster than $CH_3\overset{+}{C}O$ which is not found to be the case here. Brown and Jensen[27] have analysed kinetic data in terms of free and complexed ions, as well as ion-paired species for the $AlCl_3$ catalysed reactions. A more detailed kinetic study allowed evaluation of rate constants for various acylations in CF_3SO_3H. In all cases, the simple pseudo-second order rate law was obeyed. Data appear in Tables 3 and 4. Apart from cases where steric factors are likely to be important, it is clear from Table 3 that electron withdrawal in the acid used causes marked reduction in rate and *vice versa*; viz the complete inertness of CF_3CO_2H. (This property incidentally makes trifluoroacetic acid a very useful co-solvent for triflic acid.) Comparison of the reactivity of benzene and toluene indicates considerable substrate selectivity commesurate with a ρ^+ value of about −7 which compares well with previous values,[8] and implies a substantial development of positive charge in the transition state. The toluene–benzene rate ratio (151) is higher than that found in Lewis acid systems and this, together with the product ratios, argues for the mechanism depicted above (eqns 5, 6). However, complications arise in the interpretation of k_2^{obs} values due to competing protonation of the substrate

$$\mathrm{ArH} + \mathrm{HX} \overset{K_B}{\rightleftarrows} \mathrm{ArH}_2^+ + \bar{X}. \qquad (7)$$

The rate of reaction (V) is given by



$$V = k_2[\mathrm{ArH}]\left[\mathrm{R{-}C}\begin{matrix}\overset{+}{O}H \\ \\ X\end{matrix}\right]. \qquad (8)$$

It can be readily shown that

$$[\mathrm{ArH}] = [\mathrm{ArH}]_0\left\{1 + \frac{K_B'[\mathrm{HX}]}{[\mathrm{X}^-]}\right\}^{-1} \qquad (9)$$

Table 4. Second order rate constants (k_2^{obs} l mol^{-1} s^{-1}) for acylation of toluene using substituted benzoic acids in CF_3SO_3H at 25°. [equimolar (0.2 M) solution]

Substituent	10^3k_2
H	1.8 ± 0.3
H^a	1.6 ± 0.2
o-Cl	28 ± 1
m-Cl	5.6 ± 0.6
p-Cl	1.40 ± 0.07
o-Br	35 ± 4
m-Br	5.2 ± 0.4
p-Br	1.19 ± 0.12
o-NO_2	10^{-3}
m-NO_2	0.072 ± 0.002
p-NO_2	0.115 ± 0.002
p-NO_2^{a}	0.135 ± 0.01
o-OMe	$2.13 \pm 0.06 \times 10^{-3}$
m-OMe	1.5 ± 0.4
m-OMe^a	1.2 ± 0.2
p-OMe	0.98 ± 0.12
p-OMe^a	1.42 ± 0.30
o-Me	6.4 ± 0.8
m-Me	5.7 ± 0.4
p-Me	1.7 ± 0.2
p-Me^a	1.18 ± 0.18
pNH_2	0.067 ± 0.001

[a] In deuteriated solvent.

where ArH_0 is the total substrate concentration

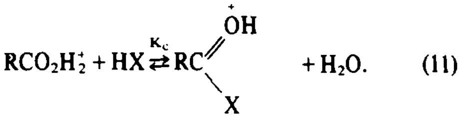
Since

$$K_B' \frac{[HX]}{[X^-]} \gg 1 \text{ (see Ref. 28)},$$

$$[ArH] \simeq [ArH_0] \frac{[\bar{X}]}{K_B'[HX]}.$$

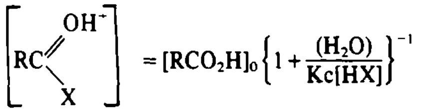
The protonated mixed anhydride is formed via the following steps:

$$RCO_2H + HX \rightarrow RCO_2H_2^+ + \bar{X} \qquad (10)$$



$$RCO_2H_2^+ + HX \overset{K_c}{\rightleftarrows} RC\begin{smallmatrix} /\!\!/ \overset{+}{O}H \\ \backslash X \end{smallmatrix} + H_2O. \qquad (11)$$

From eqn (10) and (11),



$$\left[RC\begin{smallmatrix} /\!\!/ OH^+ \\ \backslash X \end{smallmatrix}\right] = [RCO_2H]_0 \left\{1 + \frac{(H_2O)}{Kc[HX]}\right\}^{-1} \qquad (12)$$

and

$$V = \frac{k_2[\bar{X}]}{K_B'[HX]} \left\{1 + \frac{[H_2O]}{Kc[HX]}\right\}^{-1} [ArH]_0[RCO_2H]_0 \qquad (13)$$

with

$$k_2^{obs} = \frac{k_2[\bar{X}]}{K_B'[HX]} \left\{1 + \frac{(H_2O)}{K_c[HX]}\right\}^{-1} \qquad (14)$$

if K_c is very small as seems likely from the observations of Commeyras[21] eqn (14) reduces to

$$k_2^{obs} = \frac{k_2K_c}{K_B'} \frac{[\bar{X}]}{[H_2O]}. \qquad (15)$$

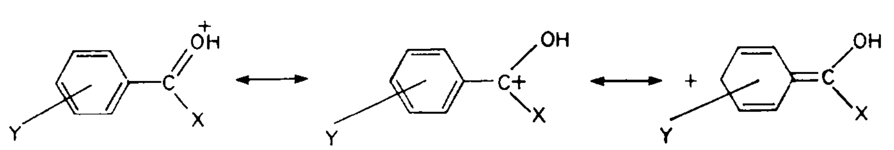
Thus when comparing the reactivity of toluene and benzene using a particular carboxylic acid, the true reactivity ratio will be given by:

$$\frac{k_2^{tol}}{k_2^{bz}} = \frac{k_2^{obs}(tol)}{k_2^{obs}(bz)} \times \frac{K_B'(tol)}{K_B'(bz)}. \qquad (16)$$

The relative basicity of toluene and benzene is still uncertain, values of $K_B'(tol)/K_{b(bz)}'^{(12)}$ in a range 10–10^3 have been reported (for a review of aromatic basicity see Ref. 29). The real substrate reactivity ratio is therefore likely to be much higher than the observed value of 151, and would lead to a substantially more negative ρ^+ value, which in turn indicates a transition state quite close in structure to the Wheland intermediate depicted in (6).

Substituent effects in the acids can be analysed by using a common substrate, toluene in this case (K_B' is constant). These effects will be manifest both on the rate constant for $RC\begin{smallmatrix} /\!\!/ OH+ \\ \backslash X \end{smallmatrix}$ attack and the equilibrium constant for its formation. The greater reactivity of acetic acid relative to formic acid can now be explained in terms of eqn (11). Since formic acid is a stronger acid than acetic acid, it will have a lower K_C than the latter. For CF_3CO_2H it is unlikely that process (11) occurs at all. The transition state for acylation is likely to resemble the σ complex where the positive charge is now delocalised around the aromatic ring (eqn 6) and substituents in the R group will have relatively little effect. Thus the overall reactivity in this case is governed by K_C. The data for the aromatic carboxylic acids appear in Table 4. No simple correlation exists with the usual Hammett substituent constants σ and σ^+ for *meta* and *para* groups. This strongly suggests that substituent effects on k_2 and K_C tend to cancel one another, resulting in a narrow range of reactivity (k_2^{obs} 1 to 6×10^{-3} mol l^{-1} s^{-1}) with the exception of the cases discussed later.

Generally K_C will be lowered by electron withdrawing substituents, whereas k_2 will be enhanced. Very low values of k_2^{obs} were found for some ortho substituents (-NO_2, OMe, NH_2). The methoxy group has a similar pK_{BH^+} value (~ −6, Ref. 30) so that of the carbonyl group (~ −7) of the carboxylic acid and both sites should be approximately equally protonated. However the basicity of the mixed anhydride should be considerably less due to the electron withdrawing effect of the triflate group. This explains the observed rate retardation but it is not possible to apportion the effects on acid and mixed anhydride protonation. Significantly, the ortho-methoxy group has a much more profound retarding effect than the meta and para substituents which would occur if inductive effects predominate. It is interesting in this context that o-methoxybenzoic acid is a much stronger base than benzoic acid in H_2SO_4[31] which indicates that the methoxy group is not significantly protonated in this medium. The very marked retardation for pNH_2 is probably due to complete protonation of the amino group. A similar trend is apparent for nitro substituents. Another very striking feature of the data is the rate *enhancement* by ortho halogen substituents (~20–30 fold rate increases over benzoic acid itself). Ortho substituents, particularly halogens have the effect of forcing



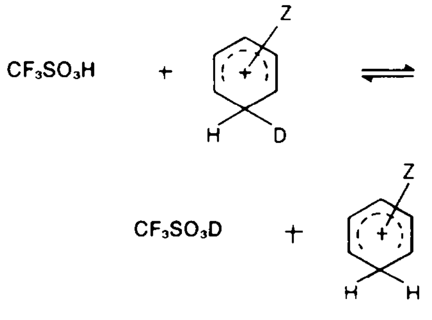
8a **8b** **8c**

the carbonyl group into a plane orthogonal to the ring thus allowing only inductive effects to operate. These are seen in the expected reduction in basicity of the ortho halogeno benzoic acids.[31] A similar reduction in basicity should occur for the mixed anhydride. Both effects would reduce the overall reaction rate which is contrary to our findings. The origin of the rate acceleration must therefore lie in the rate determining step. In the initial step, the protonated mixed anhydride will be subject to the effects of substituents in the aromatic ring by virtue of resonance, though **8b, 8c** are not considered to contribute very substantially. In addition, ortho halogens will destabilise **8** by inhibition of solvation of the charged atoms. On the other hand, in the Wheland intermediate the positive charge has been transferred to the substrate aromatic ring and the above effects in the carboxylic acid moiety largely disappear. Thus the observed rate enhancement of ortho halogens can be explained in terms of a destabilisation of the protonated mixed anhydride. The para halogeno derivatives do not suffer such destabilisation and rates are quite close to that of benzoic acid. Here the halogen will act normally and result in reduced basicity of the mixed anhydride leading to the observed small retardation.

Isotope effects are generally close to unity, although they are somewhat lower for p-OMe and p-NO_2 substituents (0.7 and 0.8 respectively). Toluene exchanges its aromatic protons very rapidly with solvent triflic acid[28] such that the effective substrate in CF_3SO_3D is d_5-toluene. Thus if proton transfer for the intermediate were rate determining this would be manifest in k_{HS}/k_{DS} values substantially greater than unity. If eqn (15) holds, then the observed isotope effect is dependent on k_2, K_C and K_B'.

$$\frac{k_2^{obs}(H)}{k_2^{obs}(D)} = \frac{k_2^H K_C^H}{k_2^D K_C^D} \cdot \frac{K_B'(D)}{K_B'(H)} \qquad (17)$$

$K_B'(H)/K_B'(D)$ is the equilibrium constant for the exchange



(18)

If the simple Bunton–Shiner[32] approach is used in the calculation of the isotope effect for (18), making use of the value of the pK_a of triflic acid of -5.9[32] to evaluate the ν_{OH}[34] and Olah's values of ν_{CH} for carbonium ions[35] than a value of ~0.9 is obtained. The value of K_C^H/K_C^D is likely to be close to unity. This equation (17) gives the isotope effect on the rate determining step at ~0.9, which indicates that the conversion of the σ intermediate to products is not rate determining. Steric factors are also clearly important as seen from the data in Table 3. Toluene undergoes acylation with mesitoic acid some 47 times slower than with p-toluic acid. For p-toluic acid, mesitylene reacts some 15 times faster than toluene. From partial rate factors for the benzoylation of aromatic compounds, mesitylene should react some 3000 times faster than toluene with p-toluic acid using data of Norman and Taylor.[36] The above discrepancy underlines the importance of steric factors in the reaction, reemphasised by the complete lack of reactivity of mesitylene with mesitoic acid. In addition, the K_B value for mesitylene is extremely large ($pK_B \sim 0.9$)[29] which means that CF_3SO_3H should compete very severely with the acylating species. The fact the p-toluic acid reacts relatively rapidly with mesitylene represents a favourable compromise between the stabilisation of the σ complex for acylation and the steric and aromatic basicity factors described above.

EXPERIMENTAL

Triflic acid (3 M chemicals) was redistilled twice from small quantities of P_2O_5 and the fraction boiling at 162–163° retained for use. The purified acid was stored in a desiccator over P_2O_5. Deuteriated triflic acid was prepared by careful addition of D_2O (99.7 at %D) to $(CF_3SO_2)_2O$ with gentle warming and exclusion of water vapour. The product was distilled from the mixture (b.p. 164–165°) and had a deuterium content of 98 at %D. All the carboxylic acids were recrystallised before use except where they were of Analar quality when they were used without further purification. Benzene and toluene were of AR grade; mesitylene was fractionally distilled prior to use.

Product analyses

A 0.5 M reaction mixture of acetic acid and toluene in CF_3SO_3H was made up. At suitable time intervals 0.2 ml aliquots were quenched in a mixture of distilled water (1.0 ml) and carbon tetrachloride (0.5 ml). The water layer was drawn off with a Pasteur pipette and the CCl_4 layer dried with a little anhydrous

Table 5. Second order rate constants k_2^{obs} ($l\ mol^{-1}\ s^{-1}$) for the reaction of toluene (0.2 M) with p-chlorobenzoic acid (0.2 M) in CF_3SO_3H at 25.0°

Time (min)	$R^{a,b}$	$10^3 k_2^{obs\,c}$	% Reaction
0	0	—	0
10	0.167	1.39	14
20	0.349	1.45	26
30	0.540	1.50	35
40	0.666	1.38	40
50	0.769	1.28	43.5
60	0.994	1.38	48

[a] Ratio of areas of product acetophenone and toluene.
[b] Correlation coefficient = 0.996.
[c] k_2^{obs} average = 1.40 ± 0.07.

$MgSO_4$. Samples of the layer were then analysed by GLC by means of a Perkin–Elmer F17 gas–liquid chromatograph using a column of 5% n-decylphthalate +5% bentone with an oven temperature of 250°. Under these conditions, the ortho, meta and para isomers had retention times of 8.5, 17.3 and 12.9 min respectively. Areas were measured and the product ratios determined (Table 2). The same procedure was adopted for the formylation reactions.

Kinetic studies

A solution of the appropriate carboxylic acid (0.2 M) was prepared at 25.0° in CF_3SO_3H. Enough toluene was injected to give an equimolar reaction solution and timing commenced. Some of the solution was rapidly transferred to an NMR tube which was placed in the thermostat bath. At suitable intervals, the NMR spectrum was rapidly run and integrated. For most reactions the amount of reaction was deduced from the ratio (R) of peak areas of product ketone to toluene. As an example for the reaction of p-chlorobenzoic acid with toluene, the product and factor methyl resonances occurred at 2.23 and 1.97 ppm. Table 5 shows typical data.

It was noteworthy that whereas the aromatic protons in toluene underwent rapid exchange with solvent such that no signals in the aromatic region were observed, no exchange occurred for the protonated carboxylic acid and the product ketone, a fact which supports the protonation of the product carboxyl or mixed anhydride, both of which would discourage solvent exchange.

The para substituted derivatives all gave simple A_2B_2 spectra for the aromatic protons.

Rate constants were reproducible to within ±6% and the variation within one run was ±5%.

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