# Friedel–Crafts Acylations of Aromatic Hydrocarbons. Part IX.[1,2] Relative Reactivities of Acetyl, Propionyl, Butyryl, Isobutyryl, Valeryl, Hexanoyl, Decanoyl, Benzoyl, and Mesitoyl Chlorides in the Acylation of Benzene and Mesitylene

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The relative reactivities in Friedel-Crafts acylations catalysed by aluminium chloride of the acyl chlorides given in the title are (i) with benzene, in ethylene dichloride solution, 1·00, 0·66, 0·54, 0·23, 0·49, 0·38, 0·38, $7·3 \times 10^{-4}$, and $2·4 \times 10^{-3}$, respectively; (ii) with benzene, in nitromethane solution, 1·00, 0·92, 0·78, 0·20, 0·64, 0·62, 0·55, 0·06, and $1·8 \times 10^{-3}$, respectively; (iii) with mesitylene, in nitromethane solution, 1·00, 0·30, 0·27, 0·18, 0·45, 0·58, 0·67, 0·35, and $1·3 \times 10^{-4}$, respectively.

THERE have been few quantitative comparisons of the reactivities of different acyl chlorides in Friedel–Crafts acylations of a common aromatic substrate.[3] Recently, however, the kinetics of aluminium chloride-catalysed acylations of toluene have been studied for several series of substituted benzoyl chlorides[4] and a series of cinnamoyl chlorides.[5] We wish to report our data on the relative reactivities of nine acyl chlorides in the Friedel–Crafts acylations of mesitylene and of benzene.

The acylation of mesitylene normally affords mixtures of monoacyl- and diacyl-mesitylenes,[1] but comparative acylation data could be obtained in nitromethane at 0°, when essentially only monoacylation takes place.[2]

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It was possible to obtain comparative data for benzene as substrate for solutions in both nitromethane and ethylene dichloride. Relative reactivities were obtained by the method of competitive acylation using the Perrier addition procedure.[6] The results of the competitive acylation experiments are given in Table 1. Average errors were estimated as *ca.* 5%.

TABLE 1

Acylation rates of various acyl chlorides relative to acetyl chloride, at 0°, with mesitylene and benzene

| | Acyl chloride (RCOCl) R | Rate (RCOCl)/Rate (AcCl) | | | |
|---|---|---|---|---|---|
| | | (*a*) Mesitylene (in $MeNO_2$) | (*b*) Benzene (in $MeNO_2$) | (*c*) Benzene (in $C_2H_4Cl_2$) | $\sigma^*$ [a] |
| 1 | Me | 1·00 | 1·00 | 1·00 | 0·000 |
| 2 | Et | 0·30 | 0·92 | 0·66 | −0·100 |
| 3 | $Pr^n$ | 0·27 | 0·78 | 0·54 | −0·115 |
| 4 | $Pr^i$ | 0·18 | 0·20 | 0·23 | −0·190 |
| 5 | $Bu^n$ | 0·45 | 0·64 | 0·49 | −0·130 |
| 6 | $n\text{-}C_5H_{11}$ | 0·58 | 0·62 | 0·38 | (−0·14) |
| 7 | $n\text{-}C_9H_{19}$ | 0·67 | 0·55 | 0·38 | (−0·14) |
| 8 | Ph | 0·35 | 0·06 | $7·3 \times 10^{-4}$ | +0·600 |
| 9 | $2,4,6\text{-}Me_3C_6H_2$ | $1·3 \times 10^{-4}$ | $1·8 \times 10^{-3}$ | $2·4 \times 10^{-3}$ | |

[a] See text. Values in parentheses are approximate values obtained from the Taft equation; the other values are taken from ref. 8.

For the acylations of benzene an increase in the chain-length of the acyl group results in a gradual decrease in reactivity, and this is more pronounced in ethylene dichloride than in nitromethane solution. There is a reasonable correlation between the logarithms of the rates of acylation relative to acetylation (1b—5b; 1c—5c in Table 1) with Taft's polar substituent constants ($\sigma^*$)[7] (which are said to be true measures of the polar effects of substituent groups) for the corresponding alkyl groups, if values of $\rho^*$ *ca.* 4·0 are used for either solvent. The phenyl group clearly does not belong to this series: for an approximate fit a relative rate value of 240 would be necessary, *i.e.* the experimental value is lower than expected by a factor of *ca.* 700. With mesitylene as substrate, in contrast, the reactivity of the acyl chlorides with n-alkyl groups decreases to a minimum with n-butyryl chloride, followed by a gradual increase for pentanoyl, hexanoyl, and decanoyl chlorides. Increasing the size of the alkyl group in an acyl chloride results in an increase of its $+I$ effect, which would reduce the reactivity of the electrophilic centre of the acylation species. In the mesitylene series, therefore, the reactivity of the acyl species appears to be anomalously high beyond n-butyrylation. One may conclude that the acylations with benzene substrate proceed essentially by the same mechanism, but that the corresponding acylations of mesitylene involve a change in mechanism as the chain-length increases. Olah and his co-workers[8] found that the relative rates of acetylation of mesitylene and benzene in nitromethane solution at 25° are 2250 : 1. The reactivities recorded in Table 1 therefore range over six powers of ten.

It has previously been reported[9] that mesitoyl chloride does not react with benzene (or some of its homologues) in the Friedel–Crafts reaction; however, acylation with the reactive substrate anisole was observed.[9] Mesitoyl chloride and the sterically similar 2,6-dimethoxybenzoyl and 2,6-dichloro-3,5-dinitrobenzoyl chlorides have now been shown to react in good yield with mesitylene under Perrier[6] conditions. These particular acylations most probably involve the intermediacy of the acyl carbonium ion.[10] The mesitoylium ion has been proposed as an intermediate in reactions other than Friedel–Crafts acylations.[11] The other acylations of mesitylene probably do not involve the 'free' carbonium ion.[4a,8,12]

In view of the evident mechanistic complexity of the present systems, the relative rate data given in Table 1 are unlikely to possess precise kinetic significance; they do, however, present the general pattern of reactivity.

## EXPERIMENTAL

I.r. spectra were measured for solutions or liquid films with a Grubb-Parsons GS 3 spectrophotometer. $^1H$ N.m.r. spectra were obtained at 60 MHz for dilute solutions in deuteriochloroform.

*G.l.c. Analyses.*—Quantitative g.l.c. analysis was carried out with the following columns: (A) 2 m × 2·2 mm i.d., packed with Apiezon L (20%) on Chromosorb P (60—80 mesh); (B) 14 in × 2·2 mm i.d., packed with Carbowax 20 M (4%) on silanised Chromosorb G (70—80 mesh); (C), as for (B), with column length 6 ft. A flame-ionisation detector, and nitrogen carrier gas, were used. Mass corrections were applied in the competitive acylation experiments; the detector responses for the various ketones were near unity, except for the isobutyryl and benzoyl derivatives. Peak integration was carried out by weighing, by triangulation, or by use of a Honeywell Precision Integrator. Kováts[13] retention indices ($I$) on columns (B) or (C) are given in Table 2, which also includes the slopes

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(*b*) of the graphs of logarithm (retention volume) against carbon number for the n-alkane.

TABLE 2

Kováts retention indices (*I*) and slopes (*b*) on Carbowax 20M

| Ketone (ArCOR) | Benzene series | Temp./ | | Mesitylene series | Temp./ | |
|---|---|---|---|---|---|---|
| R | *I* | °C | *b* | *I* | °C | *b* |
| Me | 1675 | 180 | 0·166 | 1887 | 200 | 0·148 |
| Et | 1737 | 180 | 0·166 | 1945 | 200 | 0·145 |
| $Pr^n$ | 1800 | 180 | 0·166 | 2019 | 200 | 0·145 |
| $Pr^i$ | 1718 | 180 | 0·166 | 1961 | 200 | 0·148 |
| $Bu^n$ | 1897 | 180 | 0·166 | 2010 | 156 | 0·193 |
| n-$C_5H_{11}$ | 2001 | 180 | 0·166 | 2100 | 156 | 0·193 |
| n-$C_9H_{19}$ | 2444 | 200 | 0·142 | 2547 | 200 | 0·153 |
| Ph | 2448 | 200 | 0·142 | 2498 | 200 | 0·142 |
| 2,4,6-$Me_3C_6H_2$ | 2498 | 200 | 0·142 | 2747 | 200 | 0·140 |

*Materials.*—Acetophenone, propiophenone, valerophenone, and hexanophenone were commercial samples. Other ketones were obtained by Friedel–Crafts acylations (Bouveault addition procedure [6]): n-butyrophenone, b.p. 227—230°; isobutyrophenone, b.p. 218—220°; n-decanophenone, m.p. 34—34·5° (lit.,[14] 34·3°). Acetylmesitylene, propionylmesitylene, benzoylmesitylene, and dimesityl ketone were samples obtained previously.[1]

*Isopropyl Mesityl Ketone.*—This ketone was obtained by a Perrier acylation, from mesitylene (0·05 mol), aluminium chloride (0·15 mol) and isobutyryl chloride (0·15 mol), in ethylene dichloride (10 ml) solution, the mixture being kept at 25° for 0·5 h. The ketone was obtained as an oil, b.p. 106° at 3·5 mmHg (lit.,[15] b.p. 142° at 20 mmHg), $n_D^{22}$ 1·4951, $\nu_{max.}$ (film) 1699 $cm^{-1}$ (C=O).

*Mesityl n-Pentyl Ketone.*—Mesitylene (0·025 mol) was added during 15 min to a stirred mixture of aluminium chloride (0·0275 mol), n-hexanoyl chloride (0·025 mol) and nitromethane (5 ml), kept at 0°. The reaction was allowed to proceed for 45 min., and the product was isolated in the usual way, as an *oil* (81%), b.p. 146—149° at 6·5 mmHg (Found: C, 82·3; H, 10·0. $C_{15}H_{22}O$ requires C, 82·5; H, 10·2%), $n_D^{22}$ 1·5015, $\nu_{max.}$ (film) 1704 $cm^{-1}$ (C=O).

*Mesityl Propyl Ketone.*—n-Butyryl chloride (0·05 mol) in nitromethane (2·5 ml) was added during 15 min to a stirred mixture of aluminium chloride (0·055 mol), mesitylene (0·05 mol), and nitromethane (5 ml), kept at 0°. The mixture was stirred for a further 45 min., and the product was isolated as an oil (81%), b.p. 122—124° at 5 mmHg, $n_D^{22}$ 1·5077, $\nu_{max.}$ (film) 1703 $cm^{-1}$ (C=O).

*Butyl Mesityl Ketone.*—This was obtained in a similar way as an *oil* (69%), b.p. 130—132° at 2·2 mmHg (Found: C, 81·9; H, 9·8. $C_{14}H_{20}O$ requires C, 82·25; H, 9·9%), $n_D^{22}$ 1·5039, $\nu_{max.}$ (film) 1701 $cm^{-1}$ (C=O).

*Mesityl Nonyl Ketone.*—This was made like the previous ketone (reaction time 2 h); the *product* (71%) had b.p. 184—186°/1·5 mmHg (Found: C, 83·1; H, 11·2. $C_{19}H_{30}O$ requires C, 83·1; H, 11·0%), $n_D^{22}$ 1·4940, $\nu_{max.}$ (film) 1701 $cm^{-1}$ (C=O).

2,6-*Dichloro*-3,5-*dinitrophenyl Mesityl Ketone* (with P. M. THORNE).—This ketone was obtained by Perrier acylation from equimolar proportions of 2,6-dichloro-3,5-dinitrobenzoyl chloride, mesitylene, and aluminium chloride in ethylene dichloride solution at 25°, and formed pale yellow *crystals* (from ethanol), m.p. 144° (Found: C, 49·9; H, 3·0; Cl, 18·7; N, 7·2. $C_{16}H_{12}Cl_2O_5N_2$ requires C, 50·1; H, 3·1; Cl, 18·5; N, 7·3%), $\nu_{max.}$ ($CCl_4$) 1661 $cm^{-1}$ (C=O), $\tau$ 1·64 (s, 4-H), 3·10 (s, mesityl 3- and 5-H), 7·73 (s, mesityl 4-Me), and 7·77 (s, mesityl 2- and 6-Me).

2,6-Dichloro-3,5-dinitrobenzophenone, prepared similarly, had $\nu_{max.}$ ($CCl_4$) 1676 $cm^{-1}$ (C=O), $\tau$ 1·43 (s, 4-H) and 2·00—2·63 (m, aromatic).

2,6-*Dimethoxyphenyl Mesityl Ketone* (with P. M. THORNE).—This ketone, prepared like the previous compound, formed yellow *crystals* (from ethanol), m.p. 126° (Found: C, 75·8; H, 7·3; OMe, 22·8. $C_{18}H_{20}O_3$ requires C, 76·05; H, 7·1; OMe, 21·8%), $\nu_{max.}$ ($CCl_4$) 1659 $cm^{-1}$ (C=O), $\tau$ 3·25 (s, mesityl 3- and 5-H), 2·6—2·9, 3·43, and 3·57 (m, 3-, 4- and 5-H), 6·36 (s, OMe), 7·75 (s, mesityl 4-Me), and 7·82 (s, mesityl 2- and 6-Me).

*Competitive Acylation Experiments.*—*General methods.* (i) Mesitylene (0·05 mol) was added during 15 min to a stirred mixture of acetyl chloride (0·1 mol), propionyl chloride (or other acyl chloride) (0·1 mol) and aluminium chloride (0·2 mol) in nitromethane (15 ml) at 0°. The mixture was stirred at 0° for a further 30 min, ice and 10N-hydrochloric acid were added, and the organic layer was separated (with the aid of chloroform), washed with 3N-sodium hydroxide, then water, and evaporated. The residual ketonic mixture was then analysed by g.l.c. [column (B)]; the extent of acylation was low (<20%) under these conditions.

(ii) As for (i), with benzene replacing mesitylene, and the solvent being either nitromethane or ethylene dichloride. In the latter case washing with alkali was omitted. G.l.c. analysis was carried out with column (B) or (C).

(iii) *Internal consistency experiments.* Competitive acylation experiments, carried out as before with propionyl chloride and n-butyryl chloride in nitromethane solution gave relative acylation rates (*a*) with mesitylene as substrate, 1·26; (*b*) with benzene as substrate, 1·18.

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