The Question of a Diversity of Mechanisms in Friedel-Crafts Acylation Reactions

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In a recent paper Yamase[1] adopted the view proposed earlier[2-4] that the literature data pertaining to Friedel-Crafts acylation reactions are consistent with a concept of a duality of mechanisms. According to the type and reactivity of reagent and substrate, the mechanism of acylation is considered to involve either an attack on the aromatic substrate by the acyl cation $RCO^{\oplus}$, or by the bulkier acyl halide complex RCOX, AlX_3. Evidence had been adduced earlier[3] in favour of the view that the latter mechanism operated in most "normal" acylation reactions, whilst attack by $RCO^{\oplus}$ would be likely only when steric circumstances become dominant.

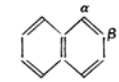
If, for instance, the acyl halide RCOX is sterically hindered, then formation of the addition complex RCOX, AlX_3 becomes energetically unfavourable*, and ionization giving the reactive acyl cation would be promoted, viz.

$$RCOX + AlX_3 \rightleftarrows RCO^{\oplus} + AlX_4^{\ominus}$$

Alternatively, when the reactive nuclear position of the substrate is sterically inaccessible, the small reagent $RCO^{\oplus}$ may be able to approach closely to the site of substitution, whilst the bulky addition complex may not. The theory of a duality of mechanisms has found a measure of general acceptance[1,6-9], whilst Brown and Jensen[6] contributed a further mechanism (i.e. involving attack by the ion-pair $(RCO^{\oplus})(AlX_4^{\ominus})$), which is not considered further here.

The data which Yamase and Goto[10,11] have recently put forward appear relevant to the concept of a duality of mechanisms. Their study of the relative reactivities of a series of acyl halides RCOX, in the presence of AlX_3, with a series of substrates, employed measurement of the "temperature of incipient reaction" (i.e. "the temperature at which the velocity of reaction becomes sufficient to cause visible bubbles (of hydrogen halide) to be evolved"), which was valuable enough in Calloway's[12] study of 1937, but which no longer can be regarded as a more than very approximate kinetic criterion.

It is of interest to consider whether the present theoretical framework of the concept of a diversity of mechanisms in the Friedel-Crafts acylation reaction would accomodate, for example, the "abnormal" substitution of naphthalene. Acylations of naphthalene[cf.4] exhibit wide variations of α- and β-isomer formation, depending on the solvent used, ranging from about 95% α- (with ethylene dichloride) to about 25% α- (with nitrobenzene). This has usually been attributed (in vague terms) to complex formation between the addition complex and solvent (S) molecules. The bulky complex RCOX, AlX_3, S would be more easily accomodated in the β-position of naphthalene[13-18]. One must admit that there is little doubt that such solvated complexes are capable of being formed under the usual reaction conditions.

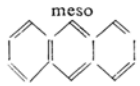


The effect of such solvation would indeed be a reduction in the electron-demand (and hence of the reactivity) of the reagent, as found experimentally. However, this clear-cut and simple role of the solvent cannot, in the present view, be supported in the light of the

* This is akin to the formation of aroyl cations from aromatic carboxylic acids (ArCOOH) on dissolution in concentrated sulphuric acid, when two ortho substituents are present. (In their absence $ArCOOH_2^{\oplus}$ is formed) (Ref. 5).

1) Y. Yamase, This Bulletin, **34**, 484 (1961).
2) J. M. Tedder, *Chem. & Ind.*, **1954**, 630.
3) P. H. Gore, ibid., **1954**, 1385.
4) P. H. Gore, *Chem. Revs.*, **55**, 229 (1955).
5) M. S. Newman, *J. Am. Chem. Soc.*, **63**, 2431 (1941).
6) H. C. Brown and F. R. Jensen, ibid., **80**, 2291 (1958).
7) C. D. Gutsche and A. J. Lauck, *Chem. & Ind.*, **1955**, 116.
8) J. Hine, "Physical Organic Chemistry", McGraw-Hill Book Company, Inc., New York (1956), p. 338.
9) F. R. Jensen, G. Marino and H. C. Brown, *J. Am. Chem. Soc.*, **81**, 3303 (1959).
10) Y. Yamase, This Bulletin, **34**, 480 (1961).
11) Y. Yamase and R. Goto, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **81**, 1906 (1960).
12) N. O. Calloway, *J. Am. Chem. Soc.*, **59**, 1474 (1937).
13) G. Baddeley, *J. Chem. Soc.*, **1949**, S. 99.
14) E. Berliner, "Organic Reactions", Vol. 5, John Wiley & Sons, Inc., New York (1949), p. 229.
15) G. Chiurdoglu and P. J. C. Fierens, *Bull. soc. chim. France*, [5] **17**, D27 (1950).
16) L. Chopin, ibid., [4] **35**, 610 (1924).
17) L. F. Fieser and M. Fieser, "Natural Products related to Phenanthrene", A. C. S. Monograph No. 70, Reinhold Publishing Corporation, New York (1949) p. 87.
18) S. M. Rivkin, *Zhur. Obshchei Khim.*, **5**, 277 (1935).

following: 1) If in nitrobenzene a bulky acylating complex is formed, why does concurrent α-substitution proceed in naphthalene, sometimes to the extent of 40%? Why can anthracene be acylated in this same solvent in its sterically hindered *meso*-position, as with benzoyl chloride in 79% yield[19], or with cinnamoyl chloride in 52% yield[4]? 2) Why

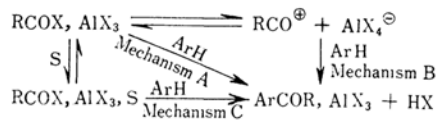


are such wide variations in isomer ratio observed with changing acyl halide? An α-/β-isomer ratio of 2.1 is obtained in the benzoylation of naphthalene in nitrobenzene, whilst under identical experimental conditions acetylation gives an isomer ratio of 0.5[13]. 3) How can appreciable β-substitution be explained in solvents such as carbon disulphide (e.g. 65% in acetylation[20]), which cannot readily solvate the aluminium chloride complexes. 4) An increase in temperature should result in increased substitution at the more sterically hindered position, whatever the solvent*. Data exist[4] for benzoylation of naphthalene, which show an increase in actual yield of β-naphthyl phenyl ketone from 24% (at 35°C) to 33% (at 150°C)[13].

The closely analogous pattern to the reversible sulphonation of naphthalene prompted the suggestion[3,4] that certain acylations may be reversible in polycyclic systems. In this theory "normal" substitution in these systems would depend on rapid precipitation of the ketone-catalyst addition complex from solution (as occurs, for example, in ethylene dichloride), whilst "abnormal" substitution would result from deacylation and resynthesis, occurring in the solution phase. Reversibility of acylation in substituted naphthalenes and higher polycyclics has now been established[4,21,22], but it appears to be of little importance[21,23] in the case of naphthalene itself, or one must surmise, with simple benzene derivatives.

The abnormal results, and the role of the solvent, in the acylations of naphthalene have not, therefore, been adequately accounted for. For this reason, and to explain recent data obtained by Jensen[23], an explanation has been sought[24] in terms of the alternative mechanisms, which may operate generally in an acylation system, viz. ArH/RCOX/S (where S = solvent).

Let it be assumed that the following reactions are possible, i.e. that the ketone ArCOR may be formed by any of three mechanistic pathways, (A) by means of the unsolvated acyl halide/catalyst complex (high reactivity, and of medium steric requirements), (B) by the free acyl carbonium ion (of high reactivity, and of low steric requirements), and (C) by a solvated acyl halide/catalyst complex (low reactivity, and of large steric requirements). It is further held that these mechanisms are not merely alternative possibilities, but that they may proceed simultaneously, their relative importance being a function of the reactivities of the reactants, and the solvating power of the solvent.



According to this view, then, α-substitution in naphthalene will proceed via mechanisms A and B, with the former predominating[3,4]. If the acyl halide is itself sterically hindered[3], mechanism B alone will operate. β-Substitution will take place by mechanisms A and C, with a trace only of B. Of these mechanisms C will become increasingly important in solvents of the type nitrobenzene, or with excess acyl halide. In solvents which tend to give "normal" (i.e. predominant α-) substitution, solvation is minimal, viz. mechanism A will operate mainly, and the product will be mostly α-, with some β- ketone. That portion of the reaction operating by mechanism B will tend to increase the percentage of α-ketone formed.

The use of excess benzoyl chloride in the benzoylation of naphthalene has recently been shown[23] to produce an increase in the proportion of β-isomer, and a marked decrease in overall yield. In the present view the effect of increasing the concentration of benzoyl chloride would here be to increase the contribution by mechanism C (at the expence of mechanism A), i.e. the proportion of β-isomer will increase. Also, since the solvated acyl complex is of low reactivity, the overall rate will decrease, and thus, presumably, will the overall yield in an equivalent experiment.

Toluene may be acetylated in ethylene dichloride solution[25] to give a p/o ratio = 83.4, whilst benzoylation[26] under similar experimental conditions involves a ratio = 9.6. It

* This assumes rate differences to be mainly due to changes in activation energy.

19) F. Krollpfeifer and F. Schütz, *Ber.*, **56**, 2360 (1923).
20) H. F. Bassilios, S. M. Makar and A. Y Salem, *Bull. soc. chim. France*, [5] **21**, 72 (1954).
21) P. H. Gore and R. B. Girdler, unpublished.
22) P. H. Gore, *J. Org. Chem.*, **22**, 135 (1957).
23) F. R. Jensen, *J. Am. Chem. Soc.*, **79**, 1226 (1957).
24) P. H. Gore, in "Friedel-Crafts and Allied Reactions". Ed. by G. A. Olah, Interscience Publishers, Inc., New York, in the press.
25) H. C. Brown, G. Marino and L. M. Stock, *J. Am. Chem. Soc.*, **81**, 3310 (1959).
26) H. C. Brown and G. Marino, ibid., 81, 3308 (1959).

was concluded[25] that the steric requirements for acetylation under these conditions (with a non-coplanar configuration of the methyl group in the acetylating species) are larger than those for benzoylation.

In the present theory, it is suggested that whilst mechanism C will not operate in the solvent used[25], viz. ethylene dichloride, the ortho and para positions may both be substituted by mechanisms A and B (the former always predominating). Ionization to $RCO^{\oplus}$ will be favoured in the case of benzoyl chloride, due to resonance stabilisation, and thus the contribution of mechanism B will increase in this case, resulting here in a higher percentage ortho substitution.

Increasing concentrations of excess benzoyl chloride have been reported[23] not to affect the rate of, and the percentage ortho isomer in, the benzoylation of toluene. Since mechanism C will not operate here, this result is here to be predicted.

The data obtained by Jensen[23] led him to conclude that the acylating species for his benzoylations of toluene and naphthalene are different. We would here add the conclusion, that the differences are due in these systems to different combinations of competing substitution processes.

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