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REACTIONS OF UNSATURATED ACID HALIDES—IV[1]

COMPETITIVE FRIEDEL–CRAFTS ACYLATIONS AND ALKYLATIONS OF MONOHALOGENOBENZENES BY THE BIFUNCTIONAL CINNAMOYL CHLORIDE

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Abstract—Aluminium chloride-catalysed acylations and alkylations of monohalogenobenzenes with cinnamoyl chloride has been studied. Under strictly homogeneous conditions, alkylation was increasingly favoured relative to acylation as the primary reaction along the series: benzene < fluorobenzene < bromobenzene < chlorobenzene. Changing to heterogeneous conditions (excess catalyst with CS_2 as diluent) preserved this order but primary alkylation was relatively enhanced. The addition of nitrobenzene to the homogeneous reaction restrained alkylation more than acylation.

Primary acylation may be followed by alkylation giving asymmetrical 1,3,3-triarylpropan-1-ones but the possibility that these are formed by alkylation followed by acylation is ruled out. These ketones may subsequently undergo α,β-ketonic fission.

Primary alkylation may be followed by cycliacylation producing 3-arylindan-1-ones with the halogeno substituent at the side-chain aryl group and this observation rules out their alternative mode of formation, cyclialkylation of the primary acylation product.

An example of a *para* → *meta* bromine shift is discussed.

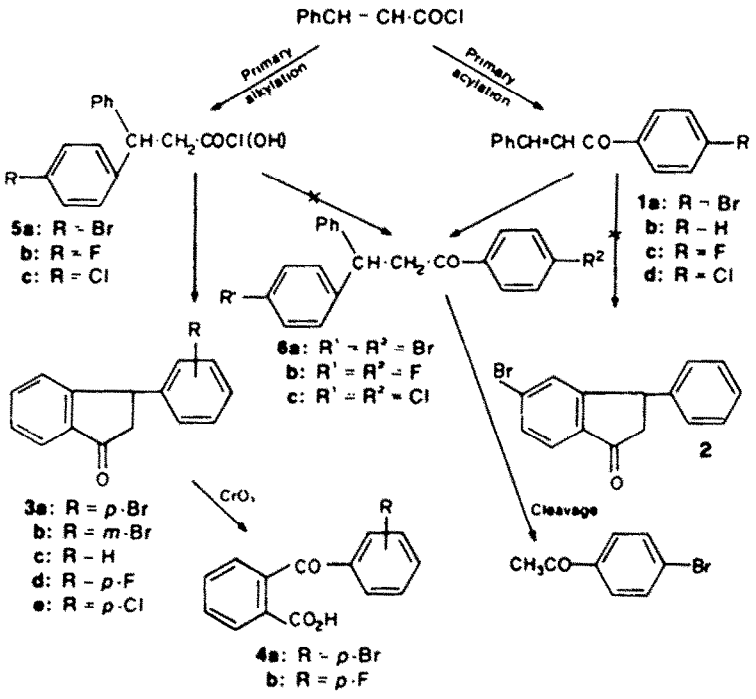
Aluminium chloride-catalysed reactions of cinnamoyl chloride with benzene were discussed in Part III.[1] This communication contains studies of reactions of the acid chloride with bromo-, fluoro- and chloro-benzenes. In view of the interest in cinnamoyl chloride as both an acylating and alkylating species, it is surprising that no previous reports have been written on its behaviour with fluoro- or chloro-benzenes. Very little is known about reactions which occur with bromobenzene.

Kohler *et al.* reported that reactions between cinnamoyl chloride, bromobenzene and aluminium chloride in carbon disulphide gave up to 25% of 4'-bromochalcone, **1a**, and 30–35% of an isomer, m.p. 60–1°, which they formulated as 5-bromo-3-phenylindan-1-one, **2**.[2] Later, Allen and Gates reported that they were unable to obtain the cyclic ketone in this manner but, nevertheless, corrected its structure to 3-(*p*-bromophenyl)-indan-1-one, **3a**.[3] A specimen of this compound, m.p. 60°, which oxidised to the known 2-(*p*-bromobenzoyl)benzoic acid, **4a**, thereby fixing the position of the Br atom, was obtained by means of a separate, aluminium chloride-catalysed cyclisation of 3 - (*p* - bromophenyl) - 3 - phenylpropionyl chloride, **5a**, which they had isolated from the products of the aforementioned reaction as a free carboxylic acid (Scheme 1).

The position of the Br atom in the indan-1-one is of crucial importance in establishing whether primary acylation or the alternative, primary alkylation, is the process responsible for the formation of the intermediate which subsequently cyclises. 5 - Bromo - 3 - phenylindan - 1 - one, **2**, would arise by cyclialkylation of 4'-bromochalcone, **1a**, the primary acylation product, whereas 3 - (*p* - bromophenyl)indan - 1 - one, **3a**, would be formed by the cycliacylation at the undeactivated nucleus of 3 - (*p* - bromophenyl) - 3 - phenylpropionyl chloride, **5a**, the primary alkylation product.

We now report that although only 5% of 4'-bromochalcone, **1a**, was isolated after cinnamoyl chloride and bromobenzene had been heated with a small excess of aluminium chloride in carbon disulphide, an experiment in which the acid chloride was heated at 95° with large excesses of both catalyst and bromobenzene but without diluent gave a substance of constant m.p. 108°, shown to be mixed crystals of 3 - (*p* - bromophenyl)indan - 1 - one, **3a**, and 3 - (*m* - bromophenyl)indan - 1 - one, **3b**, (5%). The formation of the *meta* isomer by a *para* → *meta* bromine shift is in accord with the known isomerisations of *o*-, *m*- and *p*-bromotoluenes to identical equilibrium mixtures with a preponderance of the *meta* isomer.[4] De Valois *et al.* have shown also that *para* → *meta* bromine shifts occur as a result of an intramolecular mechanism but that *para* → *ortho* shifts are intermolecular.[5] The probable reason then that the *ortho* isomer was missing from the aforementioned reaction products was that any bromine migrating intermolecularly would be trapped out by the solvent. Indeed, there was isolated in the same experiment some *p*-dibromobenzene the formation of which may be accounted for partly by this process and the remainder by the Dumreicher disproportionation of bromobenzene which gives also benzene.[6]

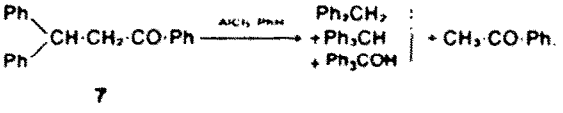
It became evident during the performance of these experiments that good reproducibility was difficult to attain and that some other compounds were formed which were not easily separated by the usual organic techniques. Olah and Olah improved the reproducibility in some otherwise unrelated Friedel–Crafts alkylations by the addition of small, measured amounts of water in order to swamp variable traces of co-catalytic water already present in the reactants.[7] We attempted to solve both problems in some later experiments by strict adherence to a procedure for producing homogeneous reaction conditions and by utilising preparative scale



Scheme 1. Friedel–Crafts reactions of cinnamoyl chloride with halogenobenzenes.

GLC for product analysis. In such experiments exactly one molecular proportion of the catalyst was mechanically shaken with a solution of the acid chloride in a large excess of halogenobenzene until only a thin film of solid (probably aluminium hydroxide) remained. The solution was then decanted and heated to the desired reaction temperature. In the case of bromobenzene, the reaction was performed at 70° for 6 hr and preparative scale GLC treatment of the products afforded 4'-bromochalcone (5.5%), **1a**, 3 - (*p* - bromophenyl)indan - 1 - one (8.2%), **3a**, and 3 - (*m* - bromophenyl)indan - 1 - one (3.4%), **3b**, the formation of which compounds has been discussed above but in addition there was obtained 3-phenylindan-1-one (5.2%), **3c**, chalcone (1.2%), **1b**, and *p*-bromoacetophenone (20%) as well as recovered cinnamic acid (29%). The two bromine-free ketones may have arisen by the loss of bromine to the substrate which is probably the case with 3-phenylindan-1-one and/or by the reaction of cinnamoyl chloride with benzene, the aforementioned disproportionation product. The second of these alternatives seems more likely to account for the formation of chalcone.

The major and perhaps the most interesting reaction was the formation of *p*-bromoacetophenone which could have arisen only in the manner which we have described in a previous communication and that is by the aluminium chloride-catalysed α,β-ketonic cleavage of a β,β-diarylpropionphenone[8] which in this case would be the unisolated 1,3 - bis - (*p* - bromophenyl) - 3 - phenylpropan - 1 - one, **6a**, the product formed by both acylation and alkylation of two molecules of bromobenzene (see below for the successful isolation of the chloro analogue). In two supplementary experiments, it was shown that the closely related 1,3,3-triphenylpropan-1-one, **7**, was cleaved in benzene but not at all in carbon disulphide by heating under reflux for 4 hr and gave in the case of benzene, acetophenone (31%) and products characteristically arising from the diphenylmethyl cation (30%) namely diphenylmethane, triphenylmethane and triphenylcarbinol (Scheme 2). The necessary aromatic environment for cleavage to occur in the above experiment is evidently provided by the excess of bromobenzene.



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Scheme 2. Cleavage of 1,3-triphenylpropan-1-one.

It is clear from the previous work of Shotter and Johnston[9] that 1,3 - bis - (*p* - bromophenyl) - 3 - phenylpropan - 1 - one, **6a**, must be formed by primary acylation followed by alkylation. If alkylation had occurred first, the product, a 3,3-diarylpropionyl chloride is expected to cyclise so readily that no intermolecular acylation can take place. It was shown that 3,3-diphenylpropionyl chloride does not acylate even toluene[9] which is considered to be more reactive towards electrophilic substitution than bromobenzene.

Analysis by means of GLC enabled 75% of the cinnamoyl chloride to be accounted for this probably cannot be improved much since most of the remainder formed an intractable tar. However, it is considered high enough for placing some confidence in estimating the ratio of yields of products formed by primary acylation and by primary alkylation (the *c*/*k* ratio). In the present case, *c*/*k*, expressed in actual percentages, is 25.5/11.6. This value is obtained by placing the yield of the ketone, **6a**, in the numerator only and by ignoring the yields of the bromine-free ketones.

The reaction of cinnamoyl chloride with fluorobenzene in the presence of a small excess of aluminium chloride

under refluxing carbon disulphide was found to give a trace of 3 - (*p* - fluorophenyl)indan - 1 - one, **3d**. By omitting the carbon disulphide and using, as a solvent, an excess of refluxing fluorobenzene there was obtained after 2 hr, 3 - (*p* - fluorophenyl)indan - 1 - one, **3d**, (33%), 1,3 - bis - (*p* - fluorophenyl) - 3 - phenylpropan - 1 - one, **6b**, (34%) and 3 - (*p* - fluorophenyl) - 3 - phenylpropionic acid, **5b**, (11%), probably contaminated with 3,3 - bis - (*p* - fluorophenyl)propionic acid formed by *β*-aryl exchange.[10] The yield of hydrogen chloride was found to be 85%. Under the same conditions, benzene gave less cyclic ketone, 3-phenylindan-1-one (8%), less primary alkylation product, 3,3-diphenylpropionic acid (5%) but more product formed by primary acylation followed by alkylation, 1,3,3 - triphenylpropan - 1 - one, **7**, (77%).[1] Fluorobenzene is the most reactive of the monohalogenobenzenes towards Friedel–Crafts acetylation[11] and benzoylation.[12] Although fluorobenzene compared with benzene shows a greater tendency to be alkylated and a lesser tendency to be acylated in the reactions under discussion, it is clear that the behaviour of fluorobenzene is fairly close to that of the parent hydrocarbon; indeed all the products are considered as arising by the same pathways as the analogous products from benzene.

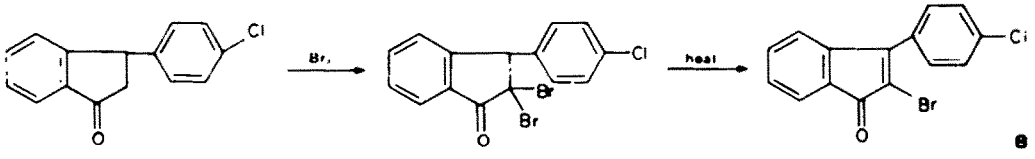
In a third experiment the aforementioned procedure for producing homogeneous conditions were employed and the solution was heated at 80° for 3.3 hr. This gave 4'-fluorochalcone (60%) as the only compound that could be isolated from the neutral products and recovered cinnamic acid (15%). Johnston and Jones found that the treatment of benzene under the same conditions, except that the period of heating was reduced to 2 hr, gave chalcone (70%) and cinnamic acid (14%).[1] Apart from demonstrating that homogeneous conditions favour acylation, these reactions again emphasise the similarity of the two aromatic substrates. The *c/k* ratio is thus 60/0—very close to that found for benzene, 70/0 where the zeros in the denominators signify that no more than a trace of primary alkylation occurred.

In order to complete our investigations, the behaviour of chlorobenzene was studied. When equimolar proportions of cinnamoyl chloride and chlorobenzene were heated for 4 hr with a slight excess of aluminium chloride in boiling carbon disulphide of sufficient volume to provide a 5-fold dilution, there was obtained a 36% yield of 3 - (*p* - chlorophenyl)indan - 1 - one, **3e**, but there was a quantitative yield of hydrogen chloride. In another experiment the carbon disulphide was omitted and an excess of chlorobenzene was used as solvent which was heated at 90° for 2 hr. Besides hydrogen chloride (67%) and cinnamic acid (14%), there was obtained a viscous oil which could not be induced to crystallize. In an attempt to separate the mixture into its pure components or their derivatives, the oil was brominated and the products distilled *in vacuo* and this afforded 2 - bromo - 3 - (*p* - chlorophenyl)ind - 1 - one, **8**, (16%) and hydrogen bromide. The *α*-bromo-indone is much more stable than *α*-halogen-free indones some of which decompose in boiling ethanol, and it is crystallised with exceptional ease. It is formed by the bromination-dehydrobromination of 3 - (*p* - chlorophenyl)indan - 1 - one (Scheme 3) in the known manner.[13] However, neither of these Friedel–Crafts experiments was particularly informative except that primary alkylation seemed to be the preferred course of the reaction. When the reaction was conducted under the aforementioned homogeneous conditions with the temperature held at 89° for 6 hr and the products analysed by means of GLC there was obtained the primary alkylation products 3 - (*p* - chlorophenyl)indan - 1 - one, **3e**, (26%), and 3 - (*p* - chlorophenyl) - 3 - phenylpropionic acid, **5c**, (27%), and the primary acylation products 4'-chlorochalcone, **1d**, (5%), and 1,3 - bis - (*p* - chlorophenyl) - 3 - phenylpropan - 1 - one, **6c**, (5%). Cinnamic acid was shown to be absent. The *c/k* ratio for chlorobenzene is thus 10/53 and is, unlike the other halogenobenzenes, very much in favour of primary alkylation compared with primary acylation.

In a supplementary experiment, the reaction was conducted under the homogeneous conditions with the temperature held at 70° for 6 hr but with the addition of an excess of nitrobenzene to ensure the complete absence of *uncombined* aluminium chloride. As expected the extent of the reaction was considerably reduced but with primary alkylation diminished more than primary acylation. The products were 3 - (*p* - chlorophenyl)indan - 1 - one, **3e**, (15%), 4'-chlorochalcone, **1d**, (6%), and recovered cinnamic acid (37%) and the *c/k* ratio 6/15.

It is concluded from the above experimentation that the order of diminishing *c/k* values for the halogenobenzenes under homogeneous conditions is benzene > fluorobenzene > bromobenzene > chlorobenzene which is the same as the order of diminishing activity in Friedel–Crafts benzoylations.[12] Stated in another way, alkylation by cinnamoyl chloride is of more account than acylation with the less active halogenobenzenes. Alkylation is also favoured in all cases by the employment of heterogeneous (excess catalyst) conditions. Further discussion of the mechanisms of these reactions is reserved awaiting the results of studies of similar reactions of nuclearly substituted cinnamoyl chlorides.

Synthesis and identification of products. The structure of 1,3 - bis - (*p* - fluorophenyl) - 3 - phenylpropan - 1 - one was confirmed by a synthesis from fluorobenzene and 4'-fluorochalcone in the presence of 1.1 mole of aluminium chloride and a stream of hydrogen chloride. No alkylation occurred without the hydrogen chloride which behaves as a co-catalyst. In an attempt to prepare the ketone by the alternative route, the alkylation of benzene by 4,4'-difluorochalcone, there was obtained 1 - (*p* - fluorophenyl) - 3,3 - diphenylpropan - 1 - one because of the intervention of *β*-aryl exchange[14,15] and a pure specimen of the exchange product was also obtained by the alkylation of benzene by 4'-fluorochalcone. 1,3 - Bis - (*p* - chlorophenyl) - 3 - phenylpropan - 1 - one was identified by oxidation to *p* - chlorobenzophenone and *p*-chlorobenzoic acid.



Scheme 3. Bromination-dehydrobromination of 3 - (*p* - chlorophenyl)indan - 1 - one.

3 - (*p* - Fluorophenyl)indan - 1 - one was prepared by the following independent route: *p*-fluorobenzophenone was converted via a Reformatskii reaction with ethyl bromacetate and zinc into ethyl 3 - (*p* - fluorophenyl) - 3 - hydroxy - 3 - phenylpropionate which was hydrolysed to the acid and then dehydrated to 3-(*p*-fluorophenyl)cinnamic acid. This was hydrogenated with sodium amalgam in aqueous alkali to the corresponding propionic acid which, on conversion to the acid chloride, was cyclised by means of aluminium chloride to the required ketone. The propionic acid derivative could not be prepared in a pure state by the alkylation of fluorobenzene by cinnamic acid. The indentity of the ketone was further established by its absorption in the IR at 1709 cm^{-1}, characteristic of a 5-ring ketone and by its NMR spectrum which gave an AMX pattern for the alicyclic protons. The position of the fluorine atom was fixed by oxidation to the known *o*-(*p*-fluorobenzoyl)benzoic acid, **4b**, which was shown to be identical with material prepared by the aluminium chloride-catalysed reaction of fluorobenzene and phthalic anhydride.

An attempt to prepare 3 - (*p* - bromophenyl) - 3 - phenylpropionic acid by the alkylation of bromobenzene with cinnamic acid as described by Dippy and Young[10] gave instead 3,3 - bis - (*p* - bromophenyl)propionic acid due to β-aryl exchange[10] and the same phenomenon occurred with chlorobenzene.[9] However, the correct monobromo acid was secured by employing Allen and Gates' modification of the procedure.[3] When this was converted to the acid chloride and cyclised with aluminium chloride in the way described by Allen and Gates[3] there was obtained mixed crystals of 3 - (*m* - bromophenyl) - and 3 - (*p* - bromophenyl) - indan - 1 - one almost identical in composition to the aforementioned product from the Friedel–Crafts reaction of cinnamoyl chloride and bromobenzene. We believe these isomerisations which did not occur in the earlier workers' experiments are due to the enhanced catalytic activity of present day commercial aluminium chloride. Pure specimens of 3 - (*m* - bromophenyl) -, 3 - (*p* - bromophenyl) -, and 3 - (*p* - chlorophenyl) - indan - 1 - ones were therefore synthesised by a method shown to be free from halogen migration, the polyphosphoric acid-catalysed cyclialkylation of 3-bromo-, 4-bromo- and 4-chloro-chalcones respectively.[19] Although we were unable to repeat Dippy and Young's aforementioned alkylation of chlorobenzene by cinnamic acid due to β-aryl exchange,[10] the reverse synthesis, namely the alkylation of benzene by *p*-chlorocinnamic acid was successful in producing 3 - (*p* - chlorophenyl) - 3 - phenylpropionic acid.

EXPERIMENTAL

IR spectra were recorded on a Perkin Elmer 137 Infracord spectrophotometer and the NMR spectrum was measured in CCl_4 with TMS as standard on a 220 Mz instrument at UKAEA, Harwell, England.† Liquid chromatography was conducted on alumina (Brockman activity No. 1). GLC was conducted on either a Perkin Elmer F11 apparatus with a silicone gum rubber stationary phase or, for preparative scale work, on a Wilkins Aerograph Autoprep 705 apparatus containing silicone gum SE 30.

Preparation and purification of reagents and reference compounds. Cinnamoyl chloride was purified by recrystallisation from light petroleum to which a few drops of $SOCl_2$ were added. Fluorobenzene was washed free of phenol by dilute alkali before fractional distillation, the portion b.p. 84.5–85° being collected. The other aromatic substrates were also purified by fractional distillation. All derivatives of chalcone were prepared by Claisen-Schmidt condensations and had satisfactory m.ps.

3-(p-Fluorophenyl)indan-1-one. The literature method was used for the preparation of ethyl 3 - (*p* - fluorophenyl) - 3 - hydroxy - 3 - phenylpropionate[16] which was then heated under reflux for 2.5 hr with 10% NaOHaq to give, after acidification, 3 - (p - *fluorophenyl*) - 3 - *hydroxy* - 3 - *phenylpropionic acid*, m.p. 182–2.5° (dec). (Found: C, 69.0; H, 5.05; F, 7.2%. $C_{15}H_{13}FO_3$ requires: C, 69.25; H, 5.05; F, 7.3%). The acid (2.0 g) was dehydrated by heating with Ac_2O (1.2 cm^3) and fused NaOAc (0.52 g) for 3 hr under reflux. The products were diluted with water (100 cm^3) and extracted with ether. The ethereal layer was extracted with sat Na_2CO_3aq (3 × 20 cm^3) and the combined aqueous layer was acidified which gave a ppt of 3-(*p*-fluorophenyl)cinnamic acid (0.3 g), m.p. 149–50° (lit.[17] 151–2°). This acid was reduced by heating with sodium amalgam (4 g) in 40% NaOHaq (50 ml) at 90° until the evolution of H_2 ceased. Acidification of the products, then recrystallisation of the ppt (0.2 g) (light petroleum) afforded 3 - (*p* - fluorophenyl) - 3 - phenylpropionic acid m.p. 116.5–7° (lit.[17] 118°). This material was considered to be very pure, but a larger batch, sufficiently pure for the next stage, was prepared by Dippy and Young's method by the alkylation of fluorobenzene with cinnamic acid[10] and had m.p. 95–98° but its IR spectrum was almost identical with that of the pure material. The acid (1.5 g, 0.006 mole) was converted into the acid chloride with $SOCl_2$ and the crude product was stirred with $AlCl_3$ (1.0 g, 0.007 mole) and CS_2 (25 cm^3) at room temp. for 1 hr and then at reflux temperature for 2 hr. The products were poured into ice/HCl and extracted with ether (10 cm^3). The ether layer was washed with Na_2CO_3aq then with water, and dried ($MgSO_4$). Distillation under reduced pressure gave 3 - (p - *fluorophenyl*)*indan* - 1 - *one* (0.65 g, 48%), b.p. 220–30°/20 mm, m.p. 119–20° (benzene/light petroleum), ν_{max} 1709 cm^{-1} (C=O in 5-ring ketone). ^1H NMR: τ 7.4, 1H (d of d, H-2); τ 6.8, 1H (d of d, H-2 [cis to H-3]); τ 5.4, 1H (d of d, H-3) (AMX system); τ 2.2, 1H (app d, H-7); τ 2.45, 1H & 2.6, 1H (2 app ts, H-5 & 6); τ 2.75, 1H (app d, H-4); τ 2.9–3.1, 4H (m, *p*-FC_6H_4-); For AMX system: $J_{cis\ vic.}$ 8 Hz; $J_{trans\ vic.}$ 4 Hz; $J_{gem.}$ ~19 Hz. (Found: C, 79.60; H, 4.90; F, 8.60%. $C_{15}H_{11}FO$ requires: C, 79.65; H, 4.90; F, 8.40%). Oxidation with chromic oxide in AcOH gave *o*-(*p*-fluorobenzoyl)benzoic acid, m.p. 136–7.5° (lit.[18] 137–7.5°) undepressed on admixture with an authentic specimen synthesised by the Friedel–Crafts reaction of phthalic anhydride with fluorobenzene.[18]

3 - (p - *Bromophenyl*) -, 3 - (p - *chlorophenyl*) - *and* 3 - (m - *bromophenyl*) - *indan* - 1 - *ones*. These were available from previous work[19] and were made by the PPA-catalysed cyclialkylation of 4-bromo-, 4-chloro- and 3-bromo-chalcones respectively.

1 - (p - *Fluorophenyl*) - 3,3 - *diphenylpropan* - 1 - *one*. Dry HCl was passed into a mixture of 4'-fluorochalcone (0.8 g, 0.0035 mole), $AlCl_3$ (0.8 g, 0.006 mole) and benzene (25 cm^3) at 25°. After 1 hr the passage of the gas was stopped and the mixture was heated gently on a water bath for 2 hr. After the usual treatment, chromatography of the products gave 4'-fluorochalcone (0.023 g) and 1 - (p - *fluorophenyl*) - 3,3 - *diphenylpropan* - 1 - *one* (0.4 g, 38%), m.p. 119–20°, ν_{max} 1692 cm^{-1} (aryl alkyl C=O). (Found: C, 82.4; H, 5.6; F, 6.4. $C_{21}H_{17}FO$ requires: C, 82.95; H, 5.65; F, 6.25%).

1,3 - *Bis* - (p - *fluorophenyl*) - 3 - *phenylpropan* - 1 - *one*. Dry HCl was passed into a mixture of 4'-fluorochalcone (2.0 g, 0.009 mole), $AlCl_3$ (1.3 g, 0.01 mole) and fluorobenzene (10 ml) heated at 60–70° for 2 hr during which time the quickly formed ppt partly redissolved. (In an otherwise identical experiment the HCl was omitted and the ppt did not partly redissolve and the starting ketone was recovered almost quantitatively.) After the usual treatment, chromatography of the products gave 4'-fluorochalcone (0.72 g) and 1,3 - bis - (*p* - fluorophenyl) - 3 - phenylpropan - 1 - one (0.3 g, 10%), m.p. 88–9° (lit.[10] 80–1°) (EtOH/water). ν_{max} 1686 cm^{-1} (aryl alkyl C=O) (1,3,3 -

†The authors wish to thank the Science Research Council of Great Britain for a grant covering the cost of this spectroscopy.

triphenylpropan - 1 - one has ν_{max} 1686 cm^{-1}). (Found: C, 78.15; H, 4.90; F, 12.20. Calc. for $C_{21}H_{16}F_2O$: C, 78.25; H, 4.95; F, 11.80%). Oxidation with chromic oxide in AcOH gave *p*-fluorobenzoic acid, m.p. and m.m.p. 181–2°.

The preparation of this ketone was attempted as described by Joshi and Jauhar.[20] 4,4'-Difluorochalcone (1.0 g, 0.0041 mole) was stirred with $AlCl_3$ (1.0 g, 0.0075 mole) and benzene (30 cm^3) at room temperature for 3 hr. The initially formed yellow ppt slowly dissolved, but impure 1 - (*p* - fluorophenyl) - 3,3 - diphenylpropan - 1 - one, (0.95 g), m.p. 116–7°, raised to 118–9° on admixture with pure material (see above), was obtained from the dark red products.

3 - (*p* - *Bromophenyl*) - 3 - *phenylpropionic acid.* An attempt to prepare this acid by the $AlCl_3$-catalysed alkylation of bromobenzene by cinnamic acid as described by Dippy and Young[10] gave instead 3,3 - bis - (*p* - bromophenyl)propionic acid, m.p. 199–201° (lit.[21] 201–2°). The required acid was obtained by following Allen and Gates' modification[3] of the previous authors' procedure and had m.p. 110° (lit.[3] 107–8°).

Reactions of cinnamoyl chloride catalysed by excesses of aluminium chloride

(a) *With bromobenzene under carbon disulphide.* The acid chloride (5.0 g, 0.030 mole) was stirred with bromobenzene (18.0 g, 0.115 mole), CS_2 (100 ml) and $AlCl_3$ (4.4 g, 0.033 mole) for 0.5 hr and then the mixture was heated under reflux for 2 hr. The products were poured into ice/HCl and the organic layer was extracted with Na_2CO_3aq (3 × 25 ml). Acidification of the alkaline extract afforded cinnamic acid, m.p. and m.m.p. 132° (0.8 g, 18%). After the neutral portion had been steam distilled, trituration of the residue with a little EtOH gave 4'-bromochalcone (0.4 g, 5%) m.p. and m.m.p. 102–3°, (EtOH), but chromatography of the mother liquor yielded no other crystalline products.

(b) *With bromobenzene and a large excess of aluminium chloride.* A mixture of acid chloride (10.0 g, 0.060 mole), $AlCl_3$ (35.6 g, 0.267 mole) and bromobenzene (157 g, 1.0 mole) was kept at 40° for 0.5 hr then at 95° for 1.5 hr with occasional shaking. The products were worked up as in (a). Crystalline *p*-dibromobenzene collected in the condenser (4.0 g) and chromatography of the residue gave mixed crystals of 3 - (*p* - bromophenyl) - and 3 - (*m* - bromophenyl) - indan - 1 - ones (0.9 g, combined yield 5%) m.p. 108° undepressed on admixture with material synthesised from the components. No separation of the isomers could be achieved by repeated recrystallisation from EtOH or benzene/light petroleum but the IR spectrum showed that the mixture contained mainly the meta isomer.

(c) *With chlorobenzene under carbon disulphide.* The acid chloride (10.0 g, 0.060 mole) was stirred with chlorobenzene (7.0 g, 0.060 mole), $AlCl_3$ (10.0 g, 0.075 mole) and CS_2 (100 cm^3) for 1 hr and then heated under reflux for 4 hr. By titration a quantitative yield of HCl was shown to be evolved and the other products were worked up as in (a) omitting the steam distillation. Chromatography of the residue obtained after the removal of ether used to extract the neutral products, yielded 3 - (*p* - chlorophenyl)indan - 1 - one (5.2 g, 36%) m.p. and m.m.p. 78°.

(d) *With a large excess of chlorobenzene.* The acid chloride (10.5 g, 0.063 mole) was stirred with $AlCl_3$ (9.26 g, 0.069 mole) and chlorobenzene (45 g, 0.4 mole) at 26° for 1 hr and then the mixture was heated at 90° for 2 hr. The yield of HCl was 67% of theory. After working-up in the usual way, the organic layer was distilled in steam in the presence of Na_2CO_3aq. Acidification of the residual aqueous layer gave cinnamic acid (1.3 g, 14%). The residual organic layer was dried and distilled under reduced pressure and the fraction b.p. 160–220°/0.8 mm, a pale yellow oil (4.6 g), which failed to crystallise from a variety of solvents was treated portionwise with a slight excess of bromine in CCl_4. The products were distilled under reduced pressure and the fraction b.p. 180–220°/0.6 mm was accompanied by the copious evolution of HBr. This fraction completely solidified and was 2 - *bromo* - 3 - (*p* - *chlorophenyl*)*ind* - 1 - *one* m.p. 180–1° (3.2 g, 16%), orange needles (CCl_4). NMR spectrum was free from alicyclic proton signals, ν_{max} 1735 cm^{-1} (5-ring ketone with α-halogen). (Found: C, 56.35; H, 3.00; Br, 24.15; Cl, 11.45; M (Rast), 307. $C_{15}H_8BrClO$ requires: C, 56.35; H, 2.50; Br, 25.05; Cl, 11.10%; M, 319.5). Oxidation with chromic oxide in acetic acid gave *p*-chlorobenzoic acid m.p. and m.m.p. 242° (partially sublimes). *Oxime* m.p. 239° (slow dec), a fine yellow powder (toluene). (Found: C, 54.05; H, 2.80; N, 4.20; Br, 23.55; Cl, 10.50. $C_{15}H_9BrClNO$ requires: C, 53.85; H, 2.70; N, 4.20; Br, 23.90; Cl, 10.60%). The ketone closely resembled in all respects the recently described[19] 2 - chloro - 3 - (*p* - chlorophenyl)ind - 1 - one m.p. 172°. It was also very similar to 2 - *bromo* - 3 - (p - *bromophenyl*)*ind* - 1 - *one* m.p. 186° prepared for comparison by the bromination-dehydrobromination of 3 - (*p* - bromophenyl)indan - 1 - one. This formed golden yellow needles (EtOH/$CHCl_3$), NMR spectrum showed no alicyclic protons, ν_{max} 1732 cm^{-1} (α-halogeno 5-ring ketone), oxidation with chromic oxide in AcOH (1 hr at 100°) gave *p*-bromobenzoic acid m.p. and m.m.p. 252°. (Found: C, 50.10; H, 2.20; Br, 44.30; M (Rast), 290. $C_{15}H_8Br_2O$ requires: C, 49.45; H, 2.10; Br, 43.65%; M, 364). The *oxime* had m.p. 252–4° (dec), lemon yellow powder (EtOH/$CHCl_3$). (Found: C, 47.45; H, 2.65; N, 3.55; Br, 41.50; M (Rast), 348. $C_{15}H_9Br_2NO$ requires: C, 47.50; H, 2.40; N, 3.70; Br, 42.20%; M, 379).

Attempts to hydrogenate 2 - bromo - 3 - (*p* - chlorophenyl)ind - 1 - one (in order to regenerate the indan-1-one) over Raney Ni at room temperature were unsuccessful. Although the soln in EtOH became colourless when 1 molecular proportion of H_2 had been absorbed, attempts to remove the solvent after filtration even at the temperature of solid CO_2 in an atmosphere of N_2 resulted in the reappearance of the colour and the recovery of the ketone.

(e) *With fluorobenzene under carbon disulphide.* After a mixture of the acid chloride (9.0 g, 0.054 mole), fluorobenzene (6.0 g, 0.0612 mole), $AlCl_3$ (7.9 g, 0.059 mole) and CS_2 (50 ml) was stirred at room temp. for 1.5 hr, then heated under reflux for 3 hr, 3 - (*p* - fluorophenyl)indan - 1 - one m.p. and m.m.p. 119–120° (0.01 g, 0.08%) was obtained when the products were worked up as in (c).

(f) *With a large excess of fluorobenzene.* A mixture of acid chloride (9.0 g, 0.054 mole) was stirred with fluorobenzene (4.1 g, 0.43 mole) and $AlCl_3$ (7.4 g, 0.060 mole) for 1 hr and then kept at 75° for 2 hr. The yield of HCl was 85% and the other products were worked up as in (c). Acidification of the Na_2CO_3-extracts gave an oily solid (1.5 g, 11%) with an IR spectrum closely similar to that of 3 - (*p* - fluorophenyl) - 3 - phenylpropionic acid, and fractional distillation of the neutral products gave 3 - (p - fluorophenyl)indan - 1 - one (4.05 g, 33%), b.p. 215–30°/20 mm, m.p. and m.m.p. 119–120°, and 1,3 - bis - (*p* - fluorophenyl) - 3 - phenylpropan - 1 - one (5.9 g, 34%), b.p. 240–60/20 mm, m.p. and m.m.p. 88°.

Reactions of cinnamoyl chloride catalysed by one mole of aluminium chloride

(g) *With fluorobenzene.* The acid chloride (1.30 g, 0.0078 mole) and fluorobenzene (31 g, 0.32 mole) were shaken with $AlCl_3$ (1.05 g, 0.0078 mole) for 1 hr. After the addition of more fluorobenzene (36 g, 0.38 mole) the red soln was decanted from a trace of solid and then heated at 80° for 3.3 hr. The products were worked up in the usual manner and acidification of the Na_2CO_3-extracts gave cinnamic acid (0.17 g, 15%). After the removal of ether and fluorobenzene from the neutral products by distillation, the residue (1.05 g, 60%), m.p. 70–6°, after one recrystallisation, gave 4'-fluorochalcone, m.p. and m.m.p. 80.5°.

(h) *With chlorobenzene.* After the acid chloride (4.0 g, 0.024 mole) had been shaken with chlorobenzene (112.5 g, 1 mole) and $AlCl_3$ (3.21 g, 0.024 mole) for 1 hr, the red soln was decanted from a little solid, diluted with more chlorobenzene (112.5 g, 1 mole) and then kept at 89° for 6 hr. The products were worked up as in (a) including steam distillation. The acidic portion was 3 - (*p* - chlorophenyl) - 3 - phenylpropionic acid m.p. and m.m.p. (with a specimen obtained by the alkylation of benzene with *p*-chlorocinnamoyl chloride) 99–100° (lit.[10] 95°), prisms (CCl_4/light petroleum) (1.7 g, 27%). The neutral portion was distilled and the fraction b.p. 194–260°/1 mm (2.2 g) was shown by prep. scale GLC to contain (in order of elution): (i) 3 - (*p* - chlorophenyl)indan - 1 - one m.p. and m.m.p. 98° (0.27 g, (1.51 g, 26%); (ii) 4'-chlorochalcone m.p. and m.m.p. 98° (0.27 g, 5%); (iii) 1,3 - *bis* - (p - *chlorophenyl*) - 3 - *phenyl* - *propan* - 1 - *one* m.p. 105–6° (0.42 g, 5%), rosettes of fine needles (light

petroleum), ν_{max} 1679 cm^{-1} (aryl alkyl C=O). (Found: C, 70.60; H, 4.54; Cl, 20.10; M (Rast), 332. $C_{21}H_{16}Cl_2O$ requires: C, 71.00; H, 4.50; Cl, 20.00%; M, 355). Oxidation with chromic oxide in AcOH (1 hr at 100°) gave *p*-chlorobenzoic acid m.p. and m.m.p. 244° (partial sublimation) and *p*-chlorobenzophenone m.p. and m.m.p. 76° together with some CO_2 (lime-water test).

(j) *With chlorobenzene in nitrobenzene.* After the acid chloride (2.0 g, 0.012 mole) and $AlCl_3$ (1.6 g, 0.012 mole) were shaken with nitrobenzene (50 cm^3) for 1 hr, chlorobenzene (112.5 g, 1 mole) was added. The orange soln was decanted from a trace of solid and kept at 60–70° for 6 hr. The products were worked up as in (a) including steam distillation. The alkali extract afforded cinnamic acid m.p. and m.m.p. 132° (0.65 g, 37%) and distillation of the neutral products gave an oil (0.6 g) b.p. 170–190°/1.5 mm, which on trituration with light petroleum gave 4'-chlorochalcone (0.18 g, 6%), m.p. and m.m.p. 98–9°. The mother liquor on evaporation gave almost pure 3 - (*p* - chlorophenyl)indan - 1 - one (0.42 g, 15%), m.p. and m.m.p. 78° (cyclohexane).

(k) *With bromobenzene.* Cinnamoyl chloride (8 g, 0.0482 mole) and $AlCl_3$ (6.42 g, 0.0482 mole) in bromobenzene (270 g, 1.72 mole) were shaken by hand until nearly all the catalyst had dissolved (1 hr). The soln was decanted and more bromobenzene added (270 g, 1.72 mole) and the mixture was stirred at 70° for 6 hr. After the products were worked up as in (a) including the steam distillation, the alkaline extract afforded cinnamic acid m.p. and m.m.p. 132° (2.1 g, 29%). The neutral residue was distilled and the yellow oily fraction b.p. 162–180°/2 mm (5 g) was dissolved in ether and crystallised at −80°. This gave a *polymorph* of 4'-bromochalcone m.p. 101°, m.m.p. with the normal form 101–2°. The polymorph formed long colourless needles (cyclohexane); by crystallising from EtOH the normal form was obtained as pale yellow plates (0.7 g). The combined mother liquors were analysed by prep. scale GLC at 300° and the following were obtained (in order of elution): (i) *p*-bromacetophenone m.p. and m.m.p. 51° (1.79 g, 20%), (ii) 3-phenylindan-1-one m.p. and m.m.p. 78° (EtOH) (0.518 g, 5.2%), (iii) chalcone m.p. and m.m.p. 56–7° (EtOH) (0.147 g, 1.5%), (iv) 4'-bromochalcone m.p. and m.m.p. 101–2° (cyclohexane) (combined yield with material from above, 0.752 g, 5.5%), (v) 3 - (*m* - bromophenyl)indan - 1 - one m.p. and m.m.p. 115–6° (cyclohexane/light petroleum) (0.463 g, 3.4%), (vi) 3 - (*p* - bromophenyl)indan - 1 - one m.p. and m.m.p. 59–60° (1.144 g, 8.2%) and (vii) an unidentified compound m.p. 78–81° (0.189 g). The IR spectra of compounds (i)–(vi) were identical with those of authentic specimens.

Cyclisations

3 - (p - *Bromophenyl*) - 3 - *phenylpropionic acid.* The acid was converted into the acid chloride, b.p. 200°/6 mm, by treatment with $SOCl_2$. The distilled acid chloride (10 g, 0.0309 mole) was treated, as described by Allen and Gates,[3] in CS_2 (100 cm^3) with $AlCl_3$ (8 g, 0.06 mole) with the temperature kept at 10–15° whilst the catalyst was added. The mixture was then stirred at 20° for 3 hr and then worked up in the usual way. The product crystallised in stout needles or prisms (benzene/light petroleum) and was mixed crystals of mainly 3 - (*m* - bromophenyl)indan - 1 - one and some 3 - (*p* - bromophenyl)indan - 1 - one m.p. and m.m.p. 108° (see (b) above), (4.2 g, 47%).

3 - (p - *Fluorphenyl*) - 3 - *hydroxy* - 3 - *phenylpropionic acid.* The acid (2 g, 0.0078 mole) was stirred with H_2SO_4 for 0.5 hr and then poured into ice/water and extracted with ether. The ether layer was extracted with Na_2CO_3aq and acidification of the alkaline extract gave β-(*p*-fluorophenyl)cinnamic acid m.p. and m.m.p. 145–9° (0.02 g, 1.1%), needles (EtOH/water). Evaporation of the neutral fraction gave 3 - (p - *fluorophenyl*)*ind* - 1 - *one* m.p. 117–9.5° as yellow needles (EtOH) (1.2 g, 69%). It was unstable in boiling EtOH (giving a green soln) and was recrystallised by dissolving in EtOH at 30–40° and then chilling to −10°. Recrystallisation at −80° from ether gave material with an unsatisfactory m.p. It formed a dark green soln in H_2SO_4. ν_{max} 1718 cm^{-1} (5-ring ketone) and 833 cm^{-1} (s) (2 adjacent aromatic H). (Found: C, 80.60; H, 4.20; F, 8.85; M (Rast), 216. $C_{15}H_9FO$ requires: C, 80.35; H, 4.00; F, 8.35%; M, 224). The *oxime* had m.p. 129–30°, lemon-yellow prisms (cyclohexane/light petroleum), stable in hot EtOH, blood-red in H_2SO_4. (Found: N, 5.65%; M (Rast), 203. $C_{15}H_{10}FNO$ requires: N, 5.85%; M, 239).

Cleavages of ketones

1,3,3-*Triphenylpropan*-1-*one in benzene.* A mixture of the ketone (0.6 g, 0.0021 mole), benzene (20 ml) and $AlCl_3$ (0.56 g, 0.0042 mole) was heated under reflux for 4 hr. After the usual working-up procedure and the removal of benzene, the residue (0.6 g) was analysed by prep. scale GLC and was shown to contain (in order of elution): (i) acetophenone (0.078 g, 31%), (ii) diphenylmethane (0.028 g, 8%), (iii) triphenylmethane (0.047 g, 9%) m.p. and m.m.p. 95°, (iv) triphenylcarbinol (0.072 g, 13%) m.p. and m.m.p. 162° and (v) recovered starting compound (0.375 g, 63%). The identities of compounds (i)–(v) were established by the comparison of their retention times and IR spectra with those of authentic specimens.

1,3,3-*Triphenylpropan*-1-*one in carbon disulphide.* This experiment was conducted in exactly the same way as the previous experiment except that benzene was replaced by CS_2 (20 ml). The ketone was recovered quantitatively and its purity established by GLC.

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