802. *Interaction of Aromatic Ketones with Aluminium Chloride.*

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The products of interaction of aluminium chloride with the 2 : 5-di-*n*-propyl derivatives of acetophenone and propiophenone and with 2 : 5- and 2 : 4-di*iso*propylacetophenone are reported. Dealkylation accompanies isomerisation and a means is revealed of obtaining 3-alkyl- and 3 : 5-dialkyl-phenyl ketones; these reactions are compared with those obtained with 2 : 5-dimethyl- and 2 : 5-diethyl-phenyl ketones.

2 : 4- and 2 : 5-Di*iso*propylacetophenone have been prepared by acetylation of *p*-di*iso*propylbenzene below 5° in ethylene chloride and carbon disulphide respectively. Both these ketones afford acetophenone and its 4-*iso*propyl derivative when fused with aluminium chloride at 100°.

Partial dealkylation of several 4-alkylacetophenones is reported.

One of us has reported (*J.*, 1944, 232) that interaction of *o*-methyl- and *o*-ethyl-aryl ketones with excess of aluminium chloride effects mainly isomerisation (80%) and that the products are determined by the relative rates of (i) deacylation followed by reacylation, and (ii) intramolecular migration of the *o*-alkyl group to the adjacent *meta*-position. This work has been extended to include aryl ketones containing other *o*-alkyl groups and we now report the action of aluminium chloride on the 2 : 5-di-*n*-propyl derivatives of acetophenone and propiophenone and on 2 : 5- and 2 : 4-di*iso*propylacetophenone. Each of these ketones, in marked contrast to those in the earlier work, provides mainly tars by interaction at temperatures above 120° and, in consequence, a temperature of 100° was selected. The products are listed in the Table, where some obtained in the earlier work are included for comparison.

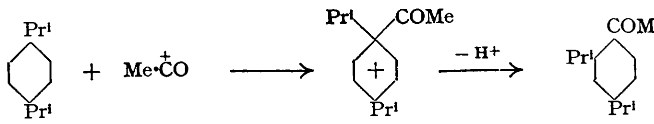
Acylation of *p*-di-*n*-propylbenzene, like that of *p*-diethylbenzene and *p*-xylene, readily affords the corresponding 2 : 5-dialkylphenyl ketone; on the other hand, 2 : 4-di*iso*propylacetophenone is obtained by interaction of *p*-di*iso*propylbenzene with acetic anhydride and aluminium chloride in boiling carbon disulphide (Newton, *J. Amer. Chem. Soc.*, 1943, **65**, 2444). We find that acetyl chloride in carbon disulphide affords the 2 : 5-isomer when the temperature of reaction is below 5° but that the 2 : 4-isomer is obtained even at these temperatures when ethylene chloride is the solvent. Both ketones were identified by deacetylation with syrupy phosphoric acid at 180° and preparation of the sulphonamides of the resulting hydrocarbons. It is unlikely that the above preparation of 2 : 4-di*iso*propylacetophenone depends on the isomerisation of the 2 : 5-isomer since this, in the presence of hydrogen and aluminium chlorides and in ethylene chloride, provides a mixture of *m*-*iso*propyl- and 3 : 5-di*iso*propyl-acetophenone; these ketones have not been described previously and were identified by oxidation to *iso*phthalic and trimesic acid respectively (see Experimental section); apparently, 2 : 4-di*iso*propylacetophenone is obtained directly from the acetylation of *p*-di*iso*propylbenzene :

Products of interaction with excess of aluminium chloride at 100° *for* 18 *hours.*

Initial ketone	Products
2 : 5-$C_6H_3Pr_2{\cdot}COMe$ ...	$C_6H_5{\cdot}COMe$ (3%) + *m*-$C_6H_4Pr{\cdot}COMe$ (43%) + 3 : 5-$C_6H_3Pr_2{\cdot}COMe$ (24%)
2 : 5-$C_6H_3Pr_2{\cdot}COEt$ ...	$C_6H_5{\cdot}COEt$ (4%) + *m*-$C_6H_4Pr{\cdot}COEt$ (36%) + 3 : 5-$C_6H_3Pr_2{\cdot}COEt$ (29%)
2 : 5-$C_6H_3Pr^i_2{\cdot}COMe$ ...	$C_6H_5{\cdot}COMe$ (27%) + *p*-$C_6H_4Pr^i{\cdot}COMe$ (27%)
*2 : 5- ,, ...	*m*- ,, (65%) + 3 : 5-$C_6H_3Pr^i_2{\cdot}COMe$ (24%)
2 : 4- ,, ...	$C_6H_5{\cdot}COMe$ (15%) + *p*- ,, (34%)

	Temp.	Time (hrs.)	Products
2 : 5-$C_6H_3Me_2{\cdot}COMe$ ...	150°	1·5	3 : 5 (77%) + 3 : 4-$C_6H_3Me_2{\cdot}COMe$ (8%)
2 : 5-$C_6H_3Et_2{\cdot}COMe$ ...	150	1·25	3 : 5-$C_6H_3Et_2{\cdot}COMe$ (88%)
p-$C_6H_4Me{\cdot}COMe$	205	1	$C_6H_5{\cdot}COMe$ (0%) + Initial ketone (80%)
p-$C_6H_4Et{\cdot}COMe$	205	1	,, (7%) + ,, (45%)
p- ,, ...	160	4	,, (2%) + ,, (75%)
p-$C_6H_4Pr{\cdot}COMe$	205	0·75	,, (7% + ,, (48%)
p- ,, ...	100	18	,, (6%) + ,, (64%)

* In Ethylene chloride at room temperature.
In each instance the rest of the material is non-volatile.



(Rings are aromatic.)

This formulation is compatible with the formation of *p*-*tert.*-butylacetophenone from *p*-di-*tert.*-butylbenzene by the action of acetyl chloride and aluminium chloride (Hennion and McLeese, *ibid.*, 1942, **64**, 2421); the *tert.*-butyl group is eliminated whereas migration of the *iso*propyl group is intramolecular. Substitution in the position *ortho* to these bulkier alkyl groups seems to encounter considerable steric hindrance.

2 : 5 -Di-*n*-propyl-acetophenone and -propiophenone behave similarly when fused with aluminium chloride at 100°. In each instance, the product of reaction distils over a wide

range of temperature and the distillate, representing 70% of the initial ketone, consists of the 3 : 5-di-*n*-propylphenyl ketone (*ca.* 38%) and the *m*-*n*-propylphenyl ketone (*ca.* 58%); these are afforded respectively by migration and elimination of the *o*-propyl group. The latter process, which provides the major product of the reaction, is not a feature of the interaction of 2 : 5-dimethylacetophenone with aluminium chloride; in this instance, the distillate is obtained over a small range of temperature and consists entirely of isomeric material; 2 : 5-diethylacetophenone, though similar in its behaviour to the 2 : 5-dimethyl derivative, does suffer some (*ca.* 3%) dealkylation.

An *o*-*iso*propyl group is still more readily eliminated than an *o*-*n*-propyl group and 2 : 5- and 2 : 4-di*iso*propylacetophenone afford only products of dealkylation, together with much tar, when fused with aluminium chloride at 100°; as mentioned above, *m*-*iso*propyl- and 3 : 5-di*iso*propyl-acetophenone are obtained in yields of 65 and 24% respectively from the 2 : 5-isomer in ethylene chloride at room temperature. These results show that ease of elimination of the alkyl group increases in the order $Me<Et<Pr^n<Pr^i$; this is compatible with the possibility that the alkyl group is eliminated as a cation. Other data in the Table show that elimination of an alkyl group is, though to a less extent, a feature of *m*- and *p*-alkylphenyl ketones.

Since acetophenone and its homologues have been alkylated by the Friedel–Crafts method (*J.*, 1949, S 229) and since dealkylation of 2 : 5-di-*n*-propyl-acetophenone and -propiophenone affords *m*-*n*-propyl-acetophenone and -propiophenone, there was the possibility that these might provide 3 : 5-dipropylphenyl ketones by interaction with propyl cations. This process does not occur since it would involve isomerisation of the propyl group and would provide 3-*n*-propyl-5-*iso*propylphenyl ketones, whereas, in fact, 3 : 5-di-*n*-propylphenyl ketones are obtained; it thus seems that these ketones, like 3 : 5-dimethyl- and 3 : 5-diethyl-phenyl ketones, are obtained from the corresponding 2 : 5-isomers by intramolecular migration of the *o*-alkyl group.

The 3 : 5-di-*n*-propyl derivatives of acetophenone and propiophenone were identified by oxidation to trimesic acid and reduction by the Clemmensen method to benzene homologues which, when polybrominated at 0° with liquid bromine in the presence of iron powder, afforded tribomo-derivatives without loss of an alkyl group; this established the configuration of the propyl groups since Hennion and Anderson (*J. Amer. Chem. Soc.*, 1946, **68**, 424) have shown that bromination under these conditions displaces secondary and tertiary but not primary alkyl groups. The *m*-*n*-propyl derivatives of acetophenone and propiophenone were identified by comparison with authentic samples.

Should the results obtained in the cases of the 2 : 5-di-*n*-propyl- and 2 : 5-di*iso*propylphenyl ketones be reproducible when the propyl and *iso*propyl groups are replaced by other normal and secondary alkyl groups, a ready means of obtaining *m*-alkyl- and 3 : 5-dialkylphenyl ketones will be available.

EXPERIMENTAL

Ketones.—2 : 5-Di-*n*-propylacetophenone was obtained by gradual addition of *p*-di-*n*-propylbenzene (60 g.) to an ice-cold mixture of aluminium chloride (78 g., 1·5 mols.) and acetyl chloride (37 g., 1·25 mols.) in ethylene chloride (400 c.c.). The product was poured on ice, the organic layer separated and dried (K_2CO_3), the solvent removed, and the residue was fractionally distilled. The required ketone (51 g.), b. p. 100—101°/0·1 mm., provided a 2 : 4-dinitrophenylhydrazone which crystallised from ethanol in orange-red needles, m. p. 75° (*J.*, 1944, 232).

2 : *5-Di*-n-*propylpropiophenone.* This ketone (55 g.), b. p. 112—116°/0·5 mm. (Found: C, 82·1; H. 9·8. Calc. for $C_{15}H_{22}O$: C, 82·5; H, 10·1%), was similarly obtained from di-*n*-propylbenzene (60 g.) and propionyl chloride (44 g.) (Baddeley and Kenner, *J.*, 1935, 303).

2 : *5-Di*iso*propylacetophenone.* *iso*Propylbenzene (50 g.), obtained by interaction of sodium-dried benzene (350 c.c.) and *iso*propyl bromide (79 g.) in the presence of aluminium chloride (10 g.) (Vogel, " Practical Organic Chemistry," p. 494, Longmans, Green and Co., London, 1948), was added to a mixture of aluminium chloride (90 g., 1·5 mols.) and acetyl chloride (42 g., 1·25 mols.) in ethylene chloride (350 c.c.). The resulting *p*-*iso*propylacetophenone (59 g.) was a pale yellow oil, b. p. 115°/10 mm., which afforded an oxime, m. p. 71° (Widman, *Ber.*, 1888, **21**, 2226), and a *semicarbazone*, m. p. 200—202° (Found: C, 66·1; H, 7·8; N, 19·3.

$C_{12}H_{17}ON$ requires C, 65·8; H, 7·8; N, 19·2%) after crystallisation from ethanol. This ketone (54 g.) in dry ether (75 c.c.) was gradually added to a solution of magnesium (12·2 g.) and methyl iodide (71 g.) in ether (250 c.c.). The mixture was stirred at room temperature for 2 hours and poured into an ice-cold solution of ammonium chloride (100 g.) in water (600 c.c.); the ethereal layer, together with two ether-extracts of the aqueous layer, was washed with water and dried (K_2CO_3). Distillation afforded 2-p-iso*propylphenylpropan-2-ol* (48 g.), b. p. 118—119°/10 mm., m. p. 38° (Found: C, 80·5; H, 9·6. $C_{12}H_{18}O$ requires C, 80·9; H, 10·1%). This alcohol (45 g.) was touched with a glass rod which had been moistened with dilute sulphuric acid and rapidly distilled under reduced pressure from an oil-bath preheated to 125°. *p-iso*Propenyl-*iso*propylbenzene (38 g.) was obtained as a mobile oil, b. p. 96—100°/12 mm.; it was reduced by hydrogen and Raney nickel in methanol to *p*-di*iso*propylbenzene (36 g.), b. p. 87—89°/15 mm. (sulphonamide, m. p. 109°; Newton, *loc. cit.*, records m. p. 110·2—110·8°), n_D^{15} 1·4910 (Ipatieff and Pines, *J. Amer. Chem. Soc.*, 1932, **54**, 674, record n_D^{20} 1·4907). A mixture of this hydrocarbon (50 g.) and acetyl chloride (27 g.) was slowly added to a vigorously stirred mixture of aluminium chloride (45 g.) and carbon disulphide (60 c.c.) at −5°; the mixture was stirred for 4 hours and the temperature allowed to rise to 5°. The mixture was decomposed with ice, and the carbon disulphide layer was separated, dried (K_2CO_3), and distilled. Initial hydrocarbon (8 g.), b. p. 55—65°/0·05 mm., and 2 : 5-*di*iso*propylacetophenone* (35 g.), b. p. 92—95°/0·1 mm., n_D^{18} 1·5120 (Found: C, 82·0; H, 9·5. $C_{14}H_{20}O$ requires C, 82·3; H, 9·8%), were obtained. This ketone afforded a *semicarbazone*, m. p. 165° (Found: C, 69·3; H, 8·6; N, 16·5. $C_{15}H_{23}ON_3$ requires C, 69·0; H, 8·8; N, 16·1%), which crystallised from ethanol. The ketone (2 c.c.) was refluxed with syrupy phosphoric acid (b. p. 180°) for 8 hours and the mixture distilled with steam; the organic material was separated, dried, and heated with concentrated sulphuric acid (2 c.c.) at 100° until a homogeneous solution was obtained. This was poured into water, and the mixture extracted with ether; the aqueous layer was neutralised with barium carbonate, filtered from barium sulphate, and freed from barium ions by addition of sodium sulphate solution. The aqueous solution was evaporated to dryness and the sodium salt heated with phosphorus pentachloride; the mixture was extracted with light petroleum, the extract washed with water, the solvent removed, and the residue heated with aqueous ammonia (*d* 0·88); the sulphamyl derivative, m. p. and mixed m. p. 110°, of p-di*iso*propylbenzene was obtained.

2 : 4-*Di*iso*propylacetophenone.* A mixture of *p*-di*iso*propylbenzene (63 g.) and acetyl chloride (33 g.) was gradually added to a vigorously stirred mixture of aluminium chloride (57 g.) and ethylene chloride (60 c.c.) at −5° and then kept overnight, the temperature gradually rising to room temperature. The mixture was decomposed with ice and worked up in the usual way; it afforded a fraction (14 g.), b. p. 69—93°/0·2 mm., 2 : 4-di*iso*propylacetophenone (39 g.), b. p. 93—97°/0·2 mm., and a residue which crystallised from light petroleum in colourless needles, m. p. 103° (Found: C, 82·1; H, 10·2%). The required ketone formed a semicarbazone, m. p. 196°, from ethanol (Newton, *loc. cit.*) and afforded 2 : 4-di*iso*propylbenzene (sulphonamide, m. p. 144—145°; cf. *idem, loc. cit.*), when deacetylated with syrupy phosphoric acid.

m-*n*-Propylpropiophenone was prepared as described by Baddeley and Kenner (*loc. cit.*); its semicarbazone melted at 132° and not at 128° as reported by them.

m-*n*-Propylacetophenone was obtained by interaction of methylmagnesium iodide and *m*-*n*-propylbenzonitrile; it afforded a *semicarbazone*, m. p. 170° (Found: C, 65·3; H, 7·8; N, 19·3. $C_{12}H_{17}ON_3$ requires C, 65·8; H, 7·8; N, 19·2%).

Interactions with Excess of Aluminium Chloride.—Procedure. A mixture of ketone and aluminium chloride (3 mols.) was heated at 100° for 18 hours; it formed a fluid melt and little chloride remained undissolved. After decomposition with ice, the mixture was extracted repeatedly with ether, and the extracts were dried (K_2CO_3) and distilled.

2 : 5-*Di*-n-*propylacetophenone.* This (50 g.) and aluminium chloride (100 g.) afforded a brown mixture which slowly evolved hydrogen chloride during the first hour and remained mobile. Ketonic material (33 g.), b. p. 55—105°/0·2 mm., was obtained; it afforded the following fractions: (i) acetophenone (0·8 g.), b. p. 53—57°/0·15 mm. (semicarbazone, m. p. and mixed m. p. 198°); (ii) *m*-*n*-propylacetophenone (17·0 g.), b. p. 70—85°/0·2 mm. (semicarbazone, m. p. and mixed m. p. 170°) [oxidation with chromic acid (Hennion and McLeese, *loc. cit.*) gave *iso*phthalic acid, identified as its dimethyl ester, m. p. and mixed m. p. 64°]; and (iii) 3 : 5-*di*-n-*propylacetophenone* (11·8 g.), b. p. 100—105°/0·2 mm. The last ketone formed a 2 : 4-*dinitrophenylhydrazone*, red needles (from ethanol), m. p. 130° (Found: C, 62·8; H, 6·3; N, 14·6. $C_{20}H_{24}O_4N_4$ requires C, 62·5; H, 6·3; N, 14·6%), and with nitric acid (Aitken, Badger, and Cook, *J.*, 1950, 331) afforded trimesic acid, m. p. 364° (trimethyl ester, m. p. and mixed m. p. 143°); oxidation with alkaline hypochlorite and with selenium dioxide and hydrogen

peroxide (Arnold and Rondesvedt, *J. Amer. Chem. Soc.*, 1945, **67**, 1265) afforded a waxy acid, m. p. 43° [Found: equiv., 202. Calc. for $(C_3H_7)_2C_6H_3\cdot CO_2H$: equiv., 206]; Clemmensen reduction gave a *hydrocarbon* which was added to a mixture of bromine and iron powder (see Hennion and Anderson, *loc. cit*), yielding a viscous oil, whose bromine content was determined by Viebock's method (*Ber.*, 1932, **65**, 586) (Found: Br, 55·7. $C_{14}H_{19}Br_3$ requires Br, 56·2%).

2 : 5-*Di*-n-*propylpropiophenone*. This (50 g.) and aluminium chloride (100 g.) afforded a brown mixture which slowly evolved hydrogen chloride during the first hour and remained mobile. Ketonic material (33·3 g.), b. p. 70—120°/0·1 mm., was obtained; it afforded (i) propiophenone (1·2 g.), b. p. 67—85°/0·1 mm. (semicarbazone, m. p. and mixed m. p. 172°); (ii) *m*-*n*-propylpropiophenone (14·6 g.), b. p. 90—100°/0·1 mm. [semicarbazone, m. p. and mixed m. p. 128° (Found: N, 18·1. Calc. for $C_{13}H_{19}ON_3$: N, 18·0%)]; and (iii) 3 : 5-*di*-n-*propylpropiophenone* (14·7 g.), b. p. 115—120°/0·1 mm., which formed a 2 : 4-*dinitrophenylhydrazone*, red needles (from acetic acid), m. p. 133° (Found: N, 14·1. $C_{21}H_{26}O_4N_4$ requires N, 14·1%), with nitric acid afforded trimesic acid, m. p. 364° (trimethyl ester, m. p. and mixed m. p. 143°), and by Clemmensen reduction gave a hydrocarbon which, as above, gave 2 : 4 : 6-*tribromo*-1 : 3 : 5-*tri*-n-*propylbenzene*, colourless needles (from ethanol), m. p. 111° (Found: C, 41·3; H, 4·8; Br, 54·5. $C_{15}H_{21}Br_3$ requires C, 40·9; H, 4·8; Br, 54·4%).

2 : 5-*Di*iso*propylacetophenone*. This (7 g.) and aluminium chloride (14 g.) afforded a brown mixture which rapidly darkened and became almost black; hydrogen chloride was evolved during the whole of the period of heating. Distillable ketonic material (2·8 g.), b. p. 45—88°/0·1 mm., and residual black tar were obtained; the former afforded (i) acetophenone (1·1 g.), b. p. 45—50°/0·1 mm., m. p. 15° (semicarbazone, m. p. and mixed m. p. 198°), and (ii) b. p. 84—88°/0·2 mm. (0·8 g.). Fraction (ii) was a mixture (semicarbazone, m. p. 157—162° after repeated recrystallisation); it contained, apparently, *p*-*iso*propylacetophenone since oxidation by chromic acid afforded terephthalic acid (dimethyl ester, m. p. and mixed m. p. 140°).

2 : 4-*Di*iso*propylacetophenone*. This (37 g.) and the chloride (74 g.) afforded a brown mixture which rapidly darkened until almost black; hydrogen chloride was evolved throughout the heating. Distillable ketonic material (16 g.) was obtained and afforded acetophenone (3·2 g.), b. p. 48—52°/0·05 mm. (semicarbazone, m. p. and mixed m. p. 198°), and *p*-*iso*propylacetophenone (10·1 g.), b. p. 80—83°/0·1 mm. [semicarbazone, m. p. and mixed m. p. 200°; with chromic acid provided terephthalic acid (dimethyl ester, m. p. and mixed m. p. 140°)].

Isomerisation of 2 : 5-*Di*iso*propylacetophenone in Ethylene Chloride at* 15°.—Finely powdered aluminium chloride (21 g.) was gradually added to a cooled solution of the ketone (20 g.) in ethylene chloride (50 c.c.); a little chloride remained undissolved. The mixture was saturated with dry hydrogen chloride and set aside at 15° for 18 hours. The mixture was decomposed with ice, and the organic layer was separated, dried (K_2CO_3), and distilled. The following fractions were obtained: (i) m-iso*Propylacetophenone* (10·3 g.), b. p. 84—90°/0·2 mm. (Found: C, 81·8; H, 9·0. $C_{11}H_{14}O$ requires C, 81·5; H, 8·6%); this afforded a *semicarbazone*, m. p. 170°, from ethanol (Found: C, 65·3; H, 7·5; N, 18·6. $C_{12}H_{17}ON_3$ requires C, 65·8; H, 7·8; N, 19·2%), which depressed the m. p. (170°) of the semicarbazone of *m*-*n*-propylacetophenone; oxidation with nitric acid afforded *iso*phthalic acid, identified as its dimethyl ester, m. p. and mixed m. p. 64°. (ii) A fraction, b. p. 95—105°/0·2 mm. (4·7 g.), which apparently contains 3 : 5-di*iso*propylacetophenone since oxidation with nitric acid gave trimesic acid which was identified as its trimethyl ester. This fraction, with 2 : 4-dinitrophenylhydrazine, provided red crystals, m. p. 117—122°, unaffected by repeated recrystallisation from ethanol and glacial acetic acid.

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