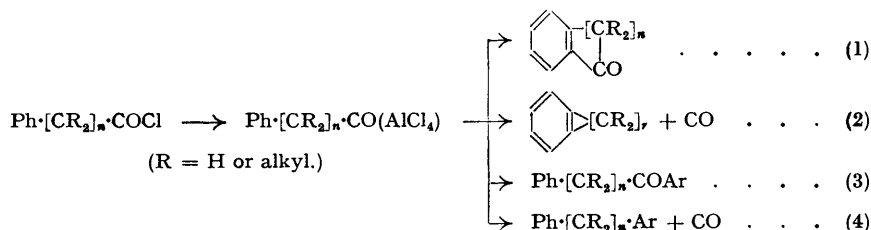


**334.** *The Reaction between Aromatic Compounds and Derivatives of Tertiary Acids. Part VI.\* The Simultaneous Formation of Open-chain and Cyclic Ketones from Some Alkylated Phenylpropionyl Chlorides.*

By EUGENE ROTHSTEIN.

Increasing proportions of open-chain ketones are produced when  $\beta$ -phenylpropionyl chloride or its derivatives methylated in the side-chain are treated with aluminium chloride in the presence of increasingly reactive aromatic derivatives. This is also observed when the concentration of the last is raised. On the other hand, increasing alkylation has the opposite effect, and with  $\beta$ -phenyl- $\alpha\alpha$ -trimethylbutyryl chloride the sole product is 2:2:3:3-tetramethylindanone.

THE inference that the preferential cyclisation usually observed with derivatives of  $\beta$ -phenylpropionyl chloride is caused by the proximity of the acyl group to the benzene nucleus (Part I, Rothstein and Saville, *J.*, 1949, 1946) leads to the reasonable conclusion that open-chain ketones should be formed in the presence of sufficiently "activated" aromatic compounds. Without necessarily implying the identity of the mechanisms of the following reactions, it is possible to envisage four products from Friedel-Crafts reactions with the appropriate acid chlorides, *viz.* :

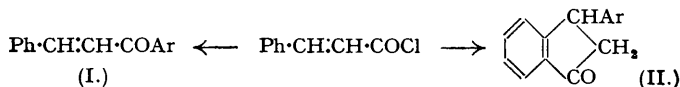


The simultaneous appearance of all four substances has not yet been encountered. Reactions (3) and (4) have been previously described (*J.*, 1949, 1950); reaction (2) will be the subject of a future communication. The present paper deals with the influence of substituent methyl groups on the relative amounts of the ketones isolated in reactions (1) and (3) where  $n = 2$ .

There are few recorded cases where open-chain ketones are formed from aralkyl acid halides. The most extensive work has been carried out with cinnamoyl chloride (for comprehensive references see Thomas, "Anhydrous Aluminium Chloride in Organic Chemistry"), the products being the chalkone (I) and the 3-aryllindan-1-one (II), the proportions depending mainly on the

\* Part V, *J.*, 1949, 1961.

substituent groups in the aryl component ArH. The course of the reaction has been examined by Kohler (*Amer. Chem. J.*, 1909, **42**, 376) but has not been fully clarified.



It is well known that  $\beta$ -phenylpropionyl chloride usually yields the indanone, but open-chain ketones are obtained by reaction with phenols (Shinoda *et al.*, *J. Pharm. Soc. Japan*, 1931, **51**, 23, 78; Mayer and Zütphen, *Ber.*, 1924, **57**, 200), or anisole (Winternitz and Mouseron, *Bull. Soc. chim.*, 1948, 567). The effect of substitution in the side-chain carrying the acid chloride group has not previously been investigated, and the results now obtained are tabulated below.

*Yield of open-chain ketones from the Friedel-Crafts reaction with alkylated  $\beta$ -phenylpropionyl chlorides.*

Expt. no.	Substituents.	Aromatic component, mols. %.*	Yield of products, %.	Open-chain ketone (mols. %) in mixture.
1	Unsubstituted	Benzene, 100	—	0.0
2	"	Anisole, 16	85.0	100.0
3	"	Toluene, 100	90.1	32.7
4	$\alpha\alpha$ -Me <sub>2</sub>	Benzene, 100	—	0.0
5	"	Anisole, 16	83.8	9.0
6	"	" 41	100.0	30.0
7	"	" 100	92.4	64.0
8	"	Toluene, 100	92.2	0.0
9	$\alpha\alpha\beta\beta$ -Me <sub>4</sub>	Benzene, 100	—	0.0
10	"	Anisole, 100	100.0	0.0

\* In benzene (where appropriate).

It is evident that an increase in the reactivity of the aromatic derivative (cf. Part II, *loc. cit.*) raises the proportion of open-chain ketone. This is particularly noticeable with  $\beta$ -phenylpropionyl chloride when the solvent is changed from benzene (complete cyclisation) to toluene or anisole (experiments 1—3). The opposite effect of successive alkylation can be observed when the reactions in pure anisole are compared. Cyclisation which is negligible in the case of  $\beta$ -phenylpropionyl chloride even when only 16% of anisole is present is the sole reaction with  $\beta$ -phenyl- $\alpha\beta\beta$ -trimethylbutyryl chloride (experiments 2, 7, and 10). It is consistent with the second-order kinetics associated with the formation of ketones (*J.*, 1949, 1959) that an increase in the concentration of anisole results in larger proportions of the non-cyclic product although in the case of the dimethylated acid chloride no more than 64% is obtained even in pure anisole solution (experiments 5—7). No appreciable quantities of carbon monoxide were eliminated in the reactions studied in this work; this conforms with the arguments advanced in Part I that the relative rates of reaction are (1) > (3) > (4).

#### EXPERIMENTAL.

The undermentioned ketones and their derivatives were isolated in the Friedel-Crafts reactions nos. 2, 3, and 5—10. The semicarbazones were best prepared in pyridine (Hopper, *J. Roy. Tech. Coll., Glasgow*, 1929, **2**, [i], 52). This method eliminated the so-called steric effects usually encountered in highly alkylated carbonyl compounds.

*p*- $\beta$ -Phenylpropionylanisole (Jörlander, *Ber.*, 1917, **50**, 406) crystallised from ether, light petroleum (b. p. 60—80°), or absolute alcohol in thick plates, m. p. 101—102° (previous workers reported 97°) (Found: C, 80.1; H, 6.3. Calc. for C<sub>16</sub>H<sub>16</sub>O<sub>2</sub>: C, 80.0; H, 6.7%). The oxime (Pfeiffer and Negreanu, *Ber.*, 1917, **50**, 1477) had m. p. 115° after recrystallisation from 95% alcohol (Found: C, 75.5; H, 6.8; N, 5.3. Calc. for C<sub>16</sub>H<sub>17</sub>O<sub>2</sub>N: C, 75.3; H, 6.7; N, 5.5%). The semicarbazone separated from the same solvent in needles, m. p. 135° (Found: C, 68.6; H, 6.4; N, 14.2. C<sub>17</sub>H<sub>19</sub>O<sub>2</sub>N<sub>3</sub> requires C, 68.7; H, 6.4; N, 14.1%).

*p*- $\beta$ -Phenylpropionyltoluene (obtained by Burton and Ingold by a different method; *J.*, 1928, 916), b. p. 145°/0.1 mm., crystallised from light petroleum (b. p. 60—80°) and had m. p. 70—71° (Found: C, 85.3; H, 7.1. Calc. for C<sub>16</sub>H<sub>16</sub>O: C, 85.7; H, 7.2%). The oxime was recrystallised twice from dilute alcohol and then had m. p. 99° (Found: C, 80.1; H, 6.9; N, 5.7. Calc. for C<sub>16</sub>H<sub>17</sub>ON: C, 80.3; H, 7.1; N, 5.9%). The semicarbazone, crystallised from alcohol, had m. p. 138—139° (Found: C, 73.0; H, 6.9; N, 15.0. Calc. for C<sub>17</sub>H<sub>19</sub>ON<sub>3</sub>: C, 72.6; H, 6.8; N, 14.9%). Burton and Ingold (*loc. cit.*) give the m. p. for the oxime as 101°, and that of the semicarbazone as 135—137°.

$\beta$ -*p*-Anisoyl-*a*-phenylisobutane, b. p. 151°/0.1 mm. (Found: C, 80.4; H, 7.6. C<sub>18</sub>H<sub>20</sub>O<sub>2</sub> requires C, 80.6; H, 7.5%). The oxime separated from absolute alcohol in needles, m. p. 157° (Found: C, 76.1; H, 7.3; N, 5.0. C<sub>18</sub>H<sub>21</sub>O<sub>2</sub>N requires C, 76.3; H, 7.4; N, 4.9%). Recrystallisation of the semicarbazone

from 95% alcohol afforded prisms, m. p. 156—157° (Found: C, 70.0; H, 7.1; N, 12.9.  $C_{19}H_{23}O_2N_3$  requires C, 70.2; H, 7.2; N, 12.9%).

2 : 2-Dimethylindan-1-one, b. p. 64°/0.1 mm., m. p. 45—46° [after recrystallisation from light petroleum (b. p. 40—60°)] (Found: C, 82.5; H, 7.8. Calc. for  $C_{11}H_{12}O$ : C, 82.5; H, 7.8%). The m. p. of the semicarbazone was somewhat indefinite (180—203°), though any particular specimen melted sharply within this range and gave a satisfactory analysis (Found, for a sample of m. p. 203°, twice crystallised from alcohol: C, 66.3; H, 6.9; N, 19.2. Calc. for  $C_{13}H_{15}ON_3$ : C, 66.4; H, 7.0; N, 19.3%). The recorded m. p. is 209° (Haller and Bauer, *Ann. Chim.*, 1921, [ix], 16, 340). The discrepancy may be caused by the formation of geometrical isomerides. No difficulty was encountered with the *oxime* which separated from dilute alcohol in prisms, m. p. 115° (Found: C, 75.0; H, 7.6; N, 8.2.  $C_{11}H_{13}ON$  requires C, 75.4; H, 7.4; N, 8.0%).

*Friedel-Crafts Reactions.*—(2) Freshly prepared aluminium chloride powder (10 g., 3/40 mol.) was dissolved in a mixture of benzene (30 c.c.) and anisole (11 c.c.). A solution of  $\beta$ -phenylpropionyl chloride (8.4 g., 1/20 mol.) in benzene (15 c.c.) was added with stirring during an hour at room temperature. The mixture was warmed for an hour at 50°, decomposed by ice and dilute hydrochloric acid, and extracted with benzene.

(3) Toluene as the only solvent gave a homogeneous liquid only after the addition of the acid chloride. The products were indan-1-one (4 g.), b. p. 73°/0.2 mm., needles, m. p. 42°, from light petroleum (b. p. 40—60°), and *p*- $\beta$ -phenylpropionyltoluene (3.3 g.).

(5) Use of pivaloyl chloride (10 g.) led to a clear red liquid which afforded 2 : 2-dimethylindan-1-one (6.1 g.) and 2-*p*-anisoyl-1-phenylisobutane (1 g.).

(6) The acid chloride was added in anisole solution. The yields of indan-1-one and open-chain ketone were 5.7 and 4.1 g. respectively.

(7) The usual quantities gave 2.65 and 7.95 g. of the respective products. An experiment starting with 23 g. of the acid chloride led to similar yields (5.8 and 20.8 g.).

(8) The indanone (8.7 g.) was the only product from this reaction.

(10)  $\alpha\alpha\beta$ -Trimethyl- $\beta$ -phenylbutyric acid (14 g.) (from tetramethylsuccinic anhydride, Rothstein and Saboor, *J.*, 1943, 425) was converted into the acid chloride, b. p. 127—128°/7 mm. (12.2 g., 80%), by using a slight excess of thionyl chloride. The reaction in anisole solution furnished 2 : 2 : 3 : 3-tetramethylindan-1-one, b. p. 80—81°/0.1 mm. in theoretical yield (Found: C, 82.8; H, 8.7. Calc. for  $C_{13}H_{16}O$ : C, 83.0; H, 8.5%). This substance had been previously prepared by Rothstein and Saboor (*loc. cit.*) by cyclising the acid itself with concentrated sulphuric acid. They had been unable to isolate any carbonyl derivatives but with the larger quantities of the pure material now available there have been prepared a *semicarbazone*, flat prisms (from 95% alcohol), m. p. 206° (Found: C, 68.6; H, 7.5; N, 16.9.  $C_{14}H_{19}ON_3$  requires C, 68.6; H, 7.8; N, 17.1%), and an *oxime*, plates (from alcohol), m. p. 143—144° (Found: C, 77.1; H, 8.6; N, 6.9.  $C_{13}H_{17}ON$  requires C, 76.8; H, 8.4; N, 6.9%).

Analyses were by Dr. G. Weiler and Dr. F. B. Strauss of Oxford.

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[Received, February 2nd, 1951.]