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Friedel-Crafts Acylations of Some Sterically Hindered Alkylbenzenes

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Introduction

The Friedel-Crafts ketone synthesis has been applied to but few *s*-alkylbenzenes; there are no reports of such reactions with *p*-di-*s*-alkyl derivatives. Since the latter are sterically hindered with respect to the available ortho positions, have tertiary hydrogen in the side chains, which also are susceptible to rearrangement, migration and displacement in the presence of aluminum chloride, it was thought of interest to study the course of their reactions with acetyl and benzoyl chlorides. A variety of these hydrocarbons was available from previous investigations.²

We were especially interested in the possibility of acylating within the side chains since these contain labile hydrogen which might react in preference to hindered hydrogen of the ring. This was not observed, however, and it appears now that 1,4-di-*s*-alkylbenzenes substitute normally in the 2-position. Mono-*s*-alkylbenzenes react in the 4-position as expected. Reactions of *t*-butylbenzene, *p*-*s*-butyltoluene and *p*-di-*t*-butylbenzene were studied also to permit comparisons of the products with those obtained from the other hydrocarbons. An anomalous reaction was observed only with *p*-di-*t*-butylbenzene, which

terephthalic acid. Oxidation of dialkylacetophenones with dilute nitric acid yielded the corresponding 4-alkylisophthalic acids, thus proving that the previous dichromate oxidations had completely removed the acetyl group in each case. Nitric acid converted *p*-*s*-alkylacetophenones to *p*-*s*-alkylbenzoic acids. In further confirmation of the assigned structures, 2,5-di-*s*-butylacetophenone was degraded to trimellitic acid by oxidation with chromic acid followed by heating with nitric acid in a sealed tube. The *p*-alkylbenzophenones and 2,5-dialkylbenzophenones were readily converted to *p*-benzoylbenzoic acid and benzoylterephthalic acid, respectively.

The non-identity of *p*-*s*-butylacetophenone and the *p*-*t*-compound, coupled with the established identity of *p*-*s*-butylbenzoic acid with an authentic sample, serves to show that the *s*-alkyl groups are not altered in structure under the conditions of the experiments.

The various ketones are described in Table I and some of the oxidation products in Table II. These list the new compounds only. It is to be noted (Table I) that there is considerable exaltation in the molecular refractions, characteristic of compounds of this type.

TABLE I
CONSTANTS, YIELDS AND ANALYTICAL DATA FOR KETONES

Compound	B. p.		n_D^{20}	d_{20}^4	Yield, %	Mol. wt.		MR		% Carbon		% Hydrogen	
	°C.	Mm.				Calcd.	Obsd.	Calcd.	Obsd.	Calcd.	Obsd.	Calcd.	Obsd.
<i>p</i> - <i>s</i> -Butylacetophenone	134-135	11	1.5195	0.9631	74	176	172	54.03	55.51	81.81	81.75	9.09	9.11
<i>p</i> - <i>s</i> -Amylacetophenone	144-145	11	1.5150	.9555	58	190	185	58.64	59.96	82.11	82.18	9.47	9.72
<i>p</i> - <i>s</i> -Octylacetophenone	134-135	3	1.5078	.9333	68	232	227	72.50	74.08	82.76	83.15	10.34	10.37
2-Methyl-5- <i>s</i> -butylacetophenone	132-133	11	1.5180	.9588	85	190	188	58.64	60.05	82.11	81.98	9.47	9.42
2,5-Di- <i>s</i> -butylacetophenone	148-149	14	1.5056	.9316	80	232	230	72.50	73.94	82.76	82.91	10.34	10.11
2,5-Di- <i>s</i> -amylacetophenone	126-127	3	1.5052	.9278	65	260	254	81.73	83.15	83.08	83.02	10.77	10.76
<i>p</i> - <i>s</i> -Butylbenzophenone	188	9	1.5760	1.0359	88	238	238	73.52	76.03	85.71	85.52	7.56	7.80
<i>p</i> - <i>s</i> -Amylbenzophenone	188-190	5	1.5672	1.0205	60	252	249	78.13	80.69	85.72	85.76	7.94	7.82
<i>p</i> - <i>s</i> -Octylbenzophenone	212-214	5	1.5540	0.9981	73	294	287	91.99	94.40	85.71	85.80	8.84	8.78
<i>p</i> - <i>s</i> -Dodecylbenzophenone	243-245	4	1.5392	.9689	45	350	344	110.46	113.19	85.71	85.62	9.71	9.70
2,5 Di- <i>s</i> -butylbenzophenone	155	3	1.5540	.9968	60	294	284	91.99	94.51	85.71	85.60	8.84	8.86

lost one butyl group, giving *p*-*t*-butylacetophenone in 72% yield.

In order to establish structures for the various ketones, it was necessary to oxidize them to known or identifiable benzene-carboxylic acids. With sodium dichromate-sulfuric acid-acetic acid mixture the alkyl and dialkylacetophenones gave

TABLE II
OXIDATION PRODUCTS

Compound	M. p., °C.	Neutral equivalent	
		Calcd.	Obsd.
4- <i>s</i> -Butylbenzoic acid	91-92	178	176
4- <i>s</i> -Amylbenzoic acid	103-104	192	189.3
4- <i>s</i> -Butylisophthalic acid	237-238	111	112
4- <i>s</i> -Amylisophthalic acid	230-231	118	120.7

Experimental

Acetophenones.—These were prepared in 0.2- to 0.8-mole quantities after the manner described in "Organic

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Syntheses.³ The monoalkylbenzenes reacted even at -10° ; with the dialkylbenzenes it was necessary to heat to the reflux temperature of carbon disulfide for several hours. Products were fractionated through a 40-cm. column to constant n_D . *p*-*t*-Butylacetophenone from *t*-butylbenzene had b. p. $133-134^{\circ}$ (11 mm.); n_D^{20} 1.5199; d_4^{20} 0.9642; from *p*-*di-t*-butylbenzene, b. p. 134° (11 mm.); n_D^{20} 1.5195; d_4^{20} 0.9635. The two semicarbazones had identical m. p. and mixed m. p., $220-221^{\circ}$ (uncor.).

Benzophenones.—The method of Gattermann and Wieland⁴ was used. Products are semi-viscous, slightly yellow liquids. They were distilled twice from glass wool in a low side-arm Claisen flask, followed by fractionation by means of a horizontal flask molecular still.⁵

Oxidations with Dichromate.—Two-gram samples of alkyl- and dialkylacetophenones were heated at $65-75^{\circ}$ with 32 g. of sodium dichromate in 60 cc. of acetic acid containing 44 g. of sulfuric acid. After diluting with water and standing overnight, the terephthalic acid was filtered, washed and dried. Neutralization equivalent, calcd., 83; obs. 83.5. Dimethyl ester, m. p. and mixed m. p., $139-140^{\circ}$.

Oxidation of Monoalkylacetophenones with Nitric Acid.—A 6-g. sample was refluxed with 600 cc. of dilute nitric acid (d. 1.09) for from eight to forty-eight hours. Terephthalic acid was removed from the hot solution and the *p*-*s*-alkylbenzoic acid allowed to crystallize.⁶ The latter was purified by heating for four hours in 15 cc. of acetic acid containing 4 g. of tin and 1 g. of zinc dust and a little hydrochloric acid, to remove nitrated impurities. Several crystallizations from dilute alcohol then gave pure products.

Oxidation of Dialkylacetophenones with Nitric Acid.—Six-gram samples were boiled with 600 cc. of nitric acid (d. 1.09) for several days and the products purified as described above.

Trimellitic Acid.—An 11.6-g. sample of *di-s*-butylacetophenone was oxidized with 75 g. of chromic acid (added in 1-g. portions over a period of thirty-five hours) in 170 g.

(3) "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1934, Vol. XIV, p. 1.

(4) "Laboratory Methods of Organic Chemistry," The Macmillan Co., New York, N. Y., 24th ed., 1938, p. 343.

(5) Morton, "Laboratory Technique in Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1938, p. 120.

(6) *p-s*-Octylacetophenone gave only terephthalic acid.

of acetic acid. The solution was poured into ice-water and extracted three times with ether. The extract was distilled, yielding a solid residue which could not be purified. Two grams of this material was heated with 10 cc. of 1:2 nitric acid in a sealed tube for twenty-four hours. After the terephthalic acid was separated, trimellitic acid crystallized on cooling. It is very soluble in water; neutralization equivalent, calcd., 70; obs., 76.

Oxidation of Benzophenones.—When boiled with dilute nitric acid, *p-s*-butyl- and *p-s*-amylbenzophenone gave *p*-benzoylbenzoic acid, m. p. and mixed m. p. $192-193^{\circ}$ (cor.). The *s*-octyl and *s*-dodecyl derivatives were not appreciably affected in this manner. Oxidation of 3-g. samples was accomplished by heating for sixteen hours with 20 g. of potassium dichromate in 90 g. of water containing 30 g. of sulfuric acid. 2,5-Di-*s*-butylbenzophenone was oxidized with dichromate-sulfuric acid-acetic acid mixture at 40° : benzoylterephthalic acid, m. p. 283° (cor.); neutralization equivalent, calcd., 135; obs., 137.

Ketone Derivatives.—Monoalkylacetophenones yielded semicarbazones in the usual manner. Prolonged heating was required to derivatize the dialkyl compounds. The new acetophenone semicarbazones with their melting points are: *p-s*-butyl, $190-191^{\circ}$; *p-s*-amyl, $173-174^{\circ}$; *p-s*-octyl, $144-145^{\circ}$; 2-methyl-5-*s*-butyl, $114-115^{\circ}$; 2,5-*di-s*-butyl, $160-161^{\circ}$; 2,5-*di-s*-amyl, $149-150^{\circ}$. Semicarbazones could not be obtained from the benzophenones.

Summary

1. *s*-Alkyl and *p*-*di-s*-alkylbenzenes react with acetyl and benzoyl chlorides in the presence of aluminum chloride without disturbance of the alkyl groups.
2. When *p*-*di-t*-butylbenzene reacted with acetyl chloride one *t*-butyl group was displaced by acetyl.
3. Structures of the various ketones were proved by oxidation.
4. A number of new substituted acetophenones, benzophenones and benzene carboxylic acids are reported and described.

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